

TRAUMATIC SHOCK.

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## SECTION I. INTRODUCTION.

The condition known as Traumatic Shock will be considered under the following headings, viz.:

### SECTION II. DEFINITION.

III. HISTORICAL SURVEY.

IV. CAUSAL FACTORS.

V. DIFFERENTIAL DIAGNOSIS.

VI. CLINICAL SIGNS.

VII. EXPERIMENTAL TRAUMATIC SHOCK.

VIII. CENTRAL NERVOUS SYSTEM.

IX. THE BLOOD AND CIRCULATION.

X. RESPIRATION.

XI. CHANGES IN THE ADRENALS.

XII. PROGRESSIVE FALL OF BODY TEMPERATURE.

XIII. PROGNOSIS.

XIV. TREATMENT.

XV. DISCUSSION AND CONCLUSIONS.

### APPENDIX A. SHORT CASE NOTES.

#### B. CHARTS OF OPERATION CASES.

The aim of this paper is to present a critical survey of the subject. This particularly applies to the recent work that has been done on it. It is intended to analyse the clinical and experimental observations and opinions

of those who have worked in this field, to determine the causal connections of the various factors, and to endeavour to reach some general conclusion as to the etiology of the condition.

My own clinical experience of the condition is incorporated in the text of the Thesis. It relates particularly to the clinical signs, and to treatment.

One's general impression of the value of Gas and Oxygen as an anaesthetic in cases where severe shock was present was obtained from its administration to scores of cases at No. 47 C.C.S., Belgium, in October and November, 1917, while acting as anaesthetist to a surgical team there.

Out of innumerable cases of Wound Shock, observed by me during the Great War in France and Belgium, a few illustrative cases are selected and recorded in Appendix A.

A short series of graphic tracings made from readings taken during operations of blood pressure, systolic and diastolic, pulse rate, and respiration rate appears in Appendix B. These were taken at the David Lewis Northern Hospital, Liverpool, on the operation cases of Mr. Monserrat, Mr. Simpson, and Mr. Rawlinson.

## SECTION II. DEFINITION.

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It is impossible in the present state of our knowledge to frame a definition of Traumatic Shock, since the fundamental cause of this condition is unknown. One can, therefore, only give a brief word-description of what is meant by it.

Traumatic Shock is an acute condition of doubtful nature due to injury, characterised by general depression of vitality, particularly of the nervous system and circulation, and often progressing rapidly to a fatal termination.

Among the preminent features are mental apathy, diminution of muscle power, cutaneous sensation, and reflexes; circulatory failure, associated with cyanotic pallor, progressive fall of blood-pressure, slowing of the blood stream in the dilated capillaries, and loss of blood volume in active circulation; change in the reaction of the blood; rapid or slow, shallow, irregular gasping respiration; fall of body temperature.

Traumatic Shock is taken to include the general depressive states that follow trauma of any sort. Both clinical and experimental traumatic shock may occur in two main types, viz. (1) Immediate (2) Delayed. (see Clinical Signs).

Of clinical traumatic shock, there are several varieties, in all of which trauma is the common factor. (1). Severe accidental injuries form a group comprising



the emergency cases often admitted to hospitals.(2). The variety due to Gunshot Wounds in the Great War was called Wound Shock, as suggested by Cowell(224,340). Cannon(225,341)suggested the term "exaemia" to denote the loss of actively circulating blood, which was such a striking feature. Quénu(414)suggested the term "hypotensive syndrome" or "traumatic texaemia".(3). The special variety due to surgical operations is termed "Operative Shock" or "Surgical Shock". Here the effects of general anaesthesia are sometimes added to those of trauma.

Other conditions may be present in combination with Traumatic Shock. The use of a qualifying adjective is then necessary to make the meaning more precise. Haemorrhagic Shock is a combination of Traumatic Shock and haemorrhage. In Toxic Shock, infection is also present, and signs of toxaemia are the main feature. In Septic Shock, septic infection is added. In Complex Shock, which French writers in particular(see Quénu(397,414)) differentiated, several of these factors were present (see also Guyot and Jeanneney(569)). In civil life, Traumatic Shock often exists in a purer form than that in the Great War, when it was often obscured or simulated by these other acute conditions, viz. haemorrhage, infection, etc.,

Many of the conditions, however, which are often termed "shock", and which more or less resemble it and are possibly partly related to it, are yet different. In these cases, the "shock" manifested by clinical signs

forms a complication of another condition. These kinds of "shock" are excluded from the scope of this paper and comprise the following: Commotional Shock, Concussion, Cerebral and Spinal, Apoplectic "Shock", Emotional, Nervous, and Psychic Shock, Toxic and Foreign Protein "Shock", Anaphylactic "Shock", Drug "Shock", e.g. strychnin and adrenin, "Shock" due to sudden abdominal catastrophes, e.g. strangulated hernia, perforated gastric ulcer, acute haemorrhagic pancreatitis, ruptured ectopic pregnancy, parturition, corrosive poisoning, etc. Some observers have suggested that the majority of these conditions are essentially identical. Crile (505, 559) regarded them as forms of exhaustion, particularly of the "kinetic" system" (see Central Nervous System). Widal (539) and others suggested that the physical process of "colloidoclasia" was the cause (see Blood).

### SECTION III. HISTORICAL SURVEY.

In the past some of the theories of traumatic shock apparently explained its phenomena according to the accepted physiology of the time, but in time as physiological knowledge expanded, the theories were shown to be incorrect. The hypothesis of vasomotor fatigue is an example of this. Probably in the future, some of the present-day explanations will be similarly found to rest on incomplete knowledge. Moreover, the views formulated to explain traumatic shock often depended on the individual bias of the theorist. The biochemist, e.g., made a bio-chemical theory, the endocrinologist suggested an internal secretion, and so on.

#### EARLY THEORIES CONCERNING "SHOCK".

The condition of "shock" was probably first described by Le Dran in 1737 (according to Vale(25)) or by John Hunter in 1784 (according to Crile(12)), while James Little in 1795 was the first to use the term "shock" for the condition. Most of the earliest observers of "shock", e.g. William Clowes in 1568, Wieseaman in 1719, Garenggeot in 1723 (quoted by Crile(13)), and Le Dran in 1737 (quoted by Vale(25)) ascribed it to organic commotion or concussion. "Shock" was recognised as a condition probably caused by the presence of some foreign body in the wound, or in the blood, or as due to a disturbed molecular condition in the tissues (see Crile(13) and Risley(132)). The nervous system in

particular was later supposed to be the most primarily affected by the trauma. Travers in 1826 (quoted by Savory(662), Holmes(664), and Mansell Moullin(2)) suggested that reflex paralysis of the heart was the cause, as it was in syncope. Dupuytren in 1832 (quoted by Risley(132)) suggested loss of nervous fluid or energy. Delcasse in 1834 (see Crile(13)) and Risley(132)) suggested "inhibition". Trauma transmitted its effects chiefly through the bones, and thus separated the living molecules from each other, especially in the brain, spinal cord, and liver. Brown-Sequard in 1856 (see Mansell Moullin(2) and Risley(132)) suggested cerebral and spinal anaemia due to persistent reflex contraction of the capillaries of the pia mater. Eisemann (see Crile (13)) later also suggested that the injury caused a contraction of the cerebral blood-vessels, and thus anaemia, just as in syncope. Hyperaemia he supposed followed the anaemia. Fourniaux Jordan in 1864 (see Crile(13)) and Risley (132)) looked on shock as a vital "depression", chiefly of the heart, while Erichsen in 1864 also (see Crile(13)) thought it due to a sharp vibration that was transmitted through everything, probably thus causing a molecular lesion. Savory (662) (see also Mansell Moullin(2) and Risley(132)) in 1870 suggested a nervous reflex paralysis of the heart, and pointed to apparently analogous instances, such as deafness resulting from sudden fright. Gross(663) (see also Crile(13)) in 1872 considered it due to "vital depression" due to "loss of innervation".



## THE THEORY OF VASOMOTOR FATIGUE.

Among the early observers to suggest this theory were Keen, Mitchell, and Morehouse, who practised as surgeons during the American Civil War about 1864 (see Agnew(665) Crile(13), Vale(25), Risley(132) and Fraser(474)). All these theories, however, were mere suggestions, more or less vague, and unsupported by experimental evidence.

In 1872 Goltz (see Mansell Moullin(2) and Howell(618)) performed his famous experiment of tapping the abdomen of a frog vertically suspended. Standstill of the heart took place, thus demonstrating the cardio-inhibitory nerves, and splanchnic dilatation indicated the possibility of reflex vasomotor paralysis. Fisher (see Mansell Moullin(2) and Meltzer(55)) about this time suggested that this and other experiments seemed to show that reflex splanchnic paralysis with corresponding anaemia of other parts occurred in traumatic shock. Mansell Moullin(2), however, pointed out that V.M. paralysis itself, due e.g. to spinal injury or section was not always followed by death. He suggested that a generalised reflex paralysis or inhibition was the cause of "shock". Groeninger (see Crile(13) and Meltzer(55)) suggested in 1885 that exhaustion of all the nerve-centres from over-stimulation was the cause of "shock".

In 1899 Crile(17, 151) gave the results of experiments dating back to 1895. From these he elaborated the theory

of vasomotor fatigue. The pressor reflexes which resulted from afferent nerve stimulation due to the trauma, he supposed, changed later, as the trauma was continued, into depressor responses, giving a fall of B.P.. This he supposed was produced by fatigue of the vasoconstrictor centre. In this country Lockhart Mummery(30,31,32) was the chief exponent.

#### OTHER PRE-WAR THEORIES.

In 1904 Kinnemann(27) suggested a disturbance of the thermogenic function as the most primary change. Jaboulay(28) suggested irreducible haemoglobin, and Vale(25) oligæmia. In 1906 Meltzer(36,55) suggested that it was not excessive excitation but reflex inhibition, first of the functions of the spinal cord, later of the centres in the medulla.

The heart again came to be regarded as the primary factor by Blum and Boise. Blum(see Crile(12)) suggested reflex irritation of the vagus, giving arrest of the heart beat. Boise(48,56) in 1907 suggested that hyper-irritation of the entire sympathetic nervous system stimulated the VASOMOTOR NERVES, and gave contraction of the arterioles and spasmodic heart action.

The Acapnia Theory was advanced by Yandell Henderson(50,68,93,95,96,124) in 1908. Diminution of CARBON DIOXIDE in the blood and tissues(acapnia), due to rapid deep respiration reflexly excited by painful stimuli caused the signs of traumatic shock.

Exhaustion of the adrenal glands was suggested by various observers, including Bainbridge and Parkinson

(38) in 1907.

### THE GREAT WAR.

These theories gave place from 1915 onwards to new conceptions in which blood-toxaemia took a primary place. In the case of Delayed Wound Shock, numerous British-American and French observers reached this common general agreement.

The "exaemia" theory elaborated by Cannon (225,567) in particular, became the most generally accepted for the case of Delayed Shock. Toxins resulting from autolysis of the injured tissues, particularly muscle destruction, passed into the circulation. Their especial action took place on the capillary walls and produced capillary stasis followed by a series of circulatory changes developing into circulatory failure. The heart, the vasomotor, the adrenal, and possibly the respiratory factors were defensive mechanisms at first, but in the later stages failed secondarily, like the general nervous, nutritive, thermogenic functions, etc., to the failure of the circulation.

The theory of complete vasomotor fatigue was definitely excluded, but Crile (160,509) still believed that fatigue from excessive stimulation of all the cells of the body, but particularly those of the brain, liver, and adrenals (the "kinetic system") was the most primary change in Traumatic Shock. Mott (531) also thought that this fatigue of the Central Nervous System played an important part in the production of all kinds of shock. In the case of Delayed Shock, however, these changes were generally looked on as secondary to the anoxaemia

due to the circulatory failure.

In the case of Immediate Shock, however, primary nerve changes probably did take place. These were generally regarded (see Guthrie (255), Mann (347), Roger (285)) as of the nature of inhibition rather than excessive stimulation resulting in fatigue.

Fat Embolism, suggested as a primary factor by Bissell (208, 273) in 1916, and by Porter (259, 446) became differentiated as a distinct condition (see Wiggers (336), Mott (531)) which might sometimes be present along with traumatic shock.

Acapnia was seen to apply only in some cases in which marked hyperpnoea was present, e.g., the prolonged excitement stage of ether anaesthesia.



SECTION LV. CAUSAL FACTORS.

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Trauma is the only invariable antecedent condition to Traumatic Shock, and is therefore its immediate cause. But several other conditions are sometimes present, in addition to trauma, before or during the state of shock, and in these cases more than one factor is the cause. It is then necessary to distinguish as clearly as possible their effects from those resulting from the trauma. Again, these various factors, either separately or in combination, may cause a shock-like condition in the absence of trauma. Whether this shock-like condition is essentially identical with traumatic shock, as Crile (505) believed, holding that they were all different types of exhaustion, or whether traumatic shock is an entity that exists apart from these conditions, as Cannon (567) believed, still remains to be proved.

In particular, in the case of traumatic shock from accidental injuries or gunshot wounds (Wound Shock), the trauma may be associated with exposure to cold and wet, fatigue, haemorrhage, infection, excessive emotion. In some cases the degree of trauma may be too slight to account for the condition alone. In surgical or operative shock, again, in addition to the trauma of the operation, the factor of general anaesthesia is also present. This kind of shock is generally regarded as a variety of Traumatic Shock (see Quénu (397)). General

anaesthesia in itself, however, may produce a shock-like depression. The trauma may be relatively slight and not enough to account for the condition.

### I. TRAUMA.

Trauma is the one exciting cause of Traumatic Shock, as it is the only factor that is invariably present in all forms of the condition.

The nature varies. It may be mechanical, e.g. cutting, penetrating, bruising, or lacerating; physical, e.g. extreme heat and cold; or chemical, e.g. the action of corrosive poisons.

The degree varies. The degree depends on the nature, intensity, and duration of the traumatic agent, and on the extent of the surface area and depth of the tissues affected.

The degree of traumatic shock varies with the degree of the trauma, other conditions being equal. Trauma alone is not always followed by traumatic shock. A certain degree of trauma is necessary. A sufficient degree of trauma always produces traumatic shock and is, therefore, its immediate cause.

A quantitative relationship also holds, provided the conditions are constant. In his researches in 1897, Crile (14,506,655) found that apparently, in experimental traumatic shock, the degree of shock varied with the degree of severity of the trauma, i.e., the more intense the trauma, the more rapid and intense the shock, and the greater the extent of the injured surface, the greater the degree of shock. This relationship probably

also held for operative shock, according to L. Mummery (31). Here, according to Crile, bruising crushing and tearing produced more intense shock than sharp cutting. Some degree of trauma was inevitable, but the nature and extent of the trauma depended largely on the surgeon himself. In accident cases, various kinds of injuries are present, including contusions, wounds, fractures, burns and scalds, etc.. In the case of burns and scalds, the extent of the area of skin affected is more important than ~~the~~ depth.

Wound Shock was caused by all forms of gunshot wound, viz. rifle and machine-gun bullets, shrapnel and high-explosive shells, hand bombs, rifle-grenades, trench-mortar bombs, aerial bombs, etc. In this particular variety of traumatic shock, Fraser and Cowell (221) found that the nature and severity of the wounds influenced the fall of arterial pressure, which they took as the main index of the degree of shock. Trivial wounds did not lower the B.P., they might even raise it. No signs of shock developed, but only some excitement, partly depending on the temperament of the individual. Moderately severe wounds, which did not immediately endanger life, might not lower the B.P. nor give signs of shock, but after a short interval the B.P. fell progressively and Delayed Shock developed. Serious wounds, which would prove fatal unless treated at once, lowered the B.P. markedly and suddenly in ~~the~~ proportion to the severity of the injuries and temperament, and caused very definite signs of Immediate Shock. Basquette

and Moulounguet(469),however, found no evident relation between the type of wound and shock,e.g.both legs might be crushed without any sign of shock.

Associated factors,as Mann(502)pointed out,are loss of blood,exposure,e.g.of abdominal viscera,changes in the normal pressure relations on opening the paritoneal or pleural cavities,and the production of nerve reflexes. And it is possible that trauma really influences the degree of shock,not directly,but indirectly through one or other of these factors.

What is the sequence of changes following trauma?

In other words,how does trauma act to produce shock? There are several possible ways.

1.Stimulation of sensory nerves.

Some such stimulation presumably occurs on the application of trauma,particularly in parts with a rich nerve-supply.In the case of Immediate Shock,this factor probably is the cause of the condition(see Central Nervous System).But in the case of Delayed Shock,no proof has yet been established,that it produces the condition(see Central Nervous System).Many surgeons believed that it was an important factor, probably from the writings of Crile,who was the chief advocate of this view and had founded his theory of "anociation"upon it.

Suppositions were drawn from observations on the effects of trauma in support of this possibility. These observations,however,are capable of other explanations,and accordingly all inferences and



deductions from these doubtful premises are fallacious.

The nature of the trauma influenced the degree of shock, as Crile(12,159)observed. E.g. crushing and tearing were the most shock-producing. Rough handling of the tissues in surgical operations generally gave alterations in the respiration and pulse rates and blood pressure levels. The intensity and duration of the trauma seemed to Crile(511,655)to bear a direct relation to the extent of the histological changes in the Central Nervous System. If the vitality were reduced, greater histological changes occurred after the trauma. Injury of those parts of the body richest in nerve-supply(i.e. nociceptors)gave the greatest changes in arterial pressure and respiration rate(generally increase)and the most marked brain-cell changes, according to Crile (12,159,506,517,559,655)and Mummery(31). The abdomen, skin, and extremities, which were rich in nociceptors contrasted with the brain, lungs, etc.,. Crile(159) pointed out that parts used in self-defence had more noci-ceptors than the protected brain which was insensitive and had no nociceptors. Experimental destruction of one hemisphere in etherised dogs gave only a slight response of circulation and respiration, and no histological changes in the other hemisphere. Crile suggested that these changes indicated a greater degree of shock, and that the degree of shock varied directly with the richness of the nerve-supply of the injured tissue, or inversely with the phylogenetic protection of the injured tissue. Injuring of large

trunks in particular, e.g. by crushing, was supposed to give a severe degree of "shock". Local anaesthesia with novocaine by blocking the nerve-supply prevented the appearance of these changes. Crile (511, 655) also found that no histological brain-cell changes were produced by traumatization of the distal areas in a "spinal" dog. The extent of the <sup>injured</sup> surface also apparently influenced the degree of shock, as Crile (quoted by Allbutt and Rolleston (89)) observed. Here, however, several other factors are at work, e.g. possible toxic absorption from the injured tissues, loss of blood by haemorrhage. From these observations and experiments, Crile (22, 159, 511, 559, 561, 655) therefore concluded that afferent stimuli, particularly pain sensation due to the trauma, produced these changes, acting harmfully on the brain cells, and, if excessive and prolonged, fatiguing them. They wore out the sensory nerve nuclei and then the vital medullary centres.

Another interpretation, however, is more probable. These changes of so-called "shock" probably consist of reflex effects on the circulation and respiration. The cardio-inhibitory centre, the vasoconstrictor centre, and the respiratory centre are stimulated by afferent impulses and reflex changes accordingly result (see Howard (641)). The more shock-producing nature and the greater intensity of the trauma may produce greater reflex effects on the circulation and respiration. In the case of Immediate Shock, the severe or relatively severe trauma produces these reflex effects to a greater degree, and it is probable that inhibition or

depression, instead of stimulation or excitation, is responsible. The longer duration involves other causal factors, e.g. longer general exposure, loss of blood, longer anaesthesia, etc, with consequent greater circulatory failure and anoxaemia, and greater secondary changes in the brain cells. Preliminary reduction of vitality also probably acts in the same way. The hypothesis of acapnia offered an explanation in some cases, as shown by Henderson and his coworkers (360, 361, 362, 363). Trauma might produce irritation of sensory nerves and result in reflex hyperpnoea, consequent diminution of  $\text{CO}_2$  in the blood and tissues (acapnia), circulatory failure, and signs of shock (see Respiration).

#### (2) Absorption of toxins.

Trauma, besides involving some irritation of sensory nerves, also inevitably involves the destruction of tissue cells. The destroyed tissue then undergoes the processes of hydrolysis, presumably by autolytic enzymes. In many cases of traumatic shock it has been proved that toxins formed by this catabolic process pass into the circulation and give rise to the signs of shock. In cases of experimental shock due to muscle bruising in particular, this has been proved to be the main causal factor. It is probably an important factor, too, in cases where extensive tissue destruction has been produced, e.g. in Wound Shock, Cuthbert Wallace (576) noticed that shock was greater when large muscular masses were divided. (See BLOOD-Absorption of Toxins).

#### (3) Circulatory Failure.

It is probable that it is by inducing circulatory

failure in one or other of the above ways that trauma produces shock. In Immediate Shock, this circulatory failure is probably mainly due to reflex effects on the circulation from afferent nerve stimulation. It may be initiated by the same means in the early stage of Delayed Shock, but in the progressive stage it is often due mainly to toxins absorbed from the injured area. (See Blood and Circulation).

## 2. PERSONAL PREDISPOSING FACTORS.

These are sometimes present and may have considerable influence on the trend of events.

### AGE.

The aged and young children are more susceptible (see Mummery(31)), but the new-born infant, according to Crile(75), is less susceptible.

### SEX.

The female, according to Crile(75), is more susceptible from after puberty to the child-bearing period of roughly between 20 and 30 years of age, and during the menopause, but less susceptible during the child-bearing period, and after the menopause.

### NATIONALITY.

The more highly organised races are more susceptible according to Crile(loc.cit.).

### OCCUPATION.

Professional and business men are more susceptible than labourers, mechanics, and farmers, people who lead a sedentary indoor life more than those who live actively out-of-doors, (Crile loc.cit.).



EMOTIVITY.

This factor, whether inherited or acquired, has a marked influence in the production of traumatic shock.

What are ~~the~~ shock-producing effects?

Nerve-cell changes in the brain resulted after excess<sup>ive</sup> emotion, according to Crile (615), identical with those found in traumatic shock.

Blood-pressure. Increased emotion tends to hypotension. Cowell (224) found that the B.P. was raised to 140-160 mms. in soldiers exposed to danger in France, or suffering from trivial wounds if of nervous diathesis. In the phlegmatic type, the B.P. might not be raised under the same conditions. Porter (261) found the B.P. normal both in the wounded and unwounded in the French Army.

Increased adrenin secretion was found in the adrenal veins after emotion in cats, probably from sympathetic stimulation, by Cannon (196) and Elliot (105, 107).

Does excessive emotion produce shock?

(1). Excessive emotion alone may cause a shock-like condition. Crile (615) <sup>found</sup> that experimental shock was produced in rabbits and cats by subjecting them to fear.

(2). Excessive emotion in the presence of shock, it is well known may aggravate shock. While emotion remains in the excitement stage it appears either to favour or counteract shock. Later, however, when depression comes on, it accentuates shock.

Excessive emotion and slight trauma, for example, might be followed by traumatic shock. Sometimes, as Mott (571) pointed out, the shock might only come on when the patient saw the injury, and was thus presumably caused

by the emotion. It is a common observation of surgeons, too, that patients of nervous "high-strung" type withstand operation much worse than those of phlegmatic type. (See CASE 1, APPENDIX A.) According to Crile, too, the more highly organised animals suffered from experimental traumatic shock more easily and more severely. On the other hand, it is well known that excitement may counteract the effects of traumatic shock at first. A wounded man may continue fighting for a time without signs of shock, but after an interval when the excitement has died down, shock may develop. Again, depression predisposes to shock. Sir William MacCormac stated (see Allbutt's System of Med. (10, 89)) that the wounded of a defeated army were more prone to shock than those of the victorious army. Anxiety or fear before operation, too, favour the appearance of shock. In the case of Wound Shock in the Great War, temperament exerted a considerable influence. (See CASE 1, APPENDIX A.) Bosquette and Moulouguet (469) also suggested that some individual predisposition to shock explained the difference in the cases.

In the case of War Neuroses, Mott (427, 431, 435) concluded that the majority were mainly due to the emotive element, inherited or acquired, and that commotional shock, or true "shell-shock" was rare. Even if the soldier had no inherited predisposition to emotivity, still he might become emotive under the strain of war. In war psychoneuroses, the psychogenic factor was the predominant causal agent, and these conditions were therefore functional, taking the form of Hysteria or Neurasthenia. Carver (418) found that commotional and emotional

shock gradually blended in borderland cases. Commotional Shock was probably due, according to Mott (427, 430, 431, 434), to organic changes in the brain and spinal cord, caused by atmospheric compression and decompression from the violent explosion, possibly also to actual concussion by violent contact with solid materials.

It is possible that the explanation of these effects of emotivity is two-fold. In the first place, during excitement, the concentration of the attention on another subject partly neutralises the effects of the trauma. In the second place, the increased adrenal secretion due to the excitement, may counteract the effects of the trauma. The heart-rate is increased, the B.P. raised, glucose liberated, the movements of the alimentary canal inhibited, and the coagulation-power of the blood increased, as the work of Cannon and Elliot indicated. On the other hand, in Immediate Shock when emotion aggravates the condition, it is probable that inhibition plays the leading role, as Guthrie (255) suggested.

### 3. PHYSICAL INFLUENCES.

#### EXPOSURE TO EXTERNAL COLD AND WET.

This is one of the most important causal factors in the production of traumatic shock.

#### What are the shock-producing effects?

Diminished metabolism, Lowering of body-temperature is induced both by the increased loss of heat and the diminished production of heat. With the lowering of temperature, the metabolic processes are retarded, according to Cannon (567). Thus all the body functions are depressed by its continuance.

Circulatory failure. Capillary stasis in the superficial capillaries is induced by cold. It is a common clinical observation that exposed parts of the body become "blue with cold". Gulland and Goodall (108, 113) stated that the red-count was increased in capillary blood taken from a cold finger. The viscosity of the blood is increased 3% by a fall of 1 deg. C. according to Denning and Watson (see Gulland and Goodall (110)). In consequence, the capillary flow is still further retarded. The <sup>Hydrogen</sup> H-ion concentration again is increased by low temperature, and thus again favours capillary stasis (see BLOOD-Reaction of the blood). The sequence of changes following this process and tending to circulatory failure is thus hastened. The blood-flow is further retarded, the fall of B.P. aggravated, and the body heat still more reduced. "Acidosis", moreover, may also be produced by cold, as Wright and Colebrook (301) showed.

External Cold alone may produce a shock-like condition. Experimental shock, Mann (347) showed, might be produced by extreme cold. This factor is often one of the originating conditions in the production of shock.

External Cold in the presence of shock may greatly aggravate the condition. In the case of Wound Shock, this exposure to cold was often a factor both in inducing and in augmenting the condition. It was found that wound shock was more common in wet weather than in dry. Wounded men who had become soaked and chilled might suffer from severe shock but recover rapidly on being warmed up. In operative shock similarly, chilling of the patient before, during, or after over-



operation, was supposed to be an important causal factor. In abdominal operations, especially, prolonged exposure of the viscera presumably causes a loss of heat, and for this reason, as Mummer (31) pointed out, the element of time has an important bearing, especially in children.

#### TIME OF DAY.

In the early hours of the morning, the "vital tide" is at its lowest ebb, as Prof. John Wyllie used to remark.

#### SEASON.

In North America, the end of winter and beginning of spring, and during the heat of the summer were, according to Crile (75) the least favourable times for operation.

#### CLIMATE AND ALTITUDE.

According to Crile (loc. cit) patients who were not acclimatised or who had not regained their normal equilibrium, were more susceptible.

### 4. PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS.

#### (a) FATIGUE FROM EXTREME EXERTION OR WANT OF SLEEP.

This factor is also very important as a causal agent.

#### What are the shock-producing effects?

It is only in so far as the effects on the central nervous system are concerned that fatigue tends to produce shock. A general nervous depression results from it. The nature of fatigue, however, can only be known when we know more of the chemistry of living matter. While sleep is the period of comparative rest, during which the anabolic processes are in excess of the catabolic (see Howell (618)), fatigue appears to be

the converse. And while the nature of sleep is explained by a number of different theories, of which the anaemia theory of Hill and Howell (618) seems most generally accepted, similarly the nature of fatigue is equally obscure. Crile, however, professed to regard fatigue as exhaustion of the "kinetic system" in the same way as traumatic shock. He (508, 553) emphasised that rest and sleep gave fundamental restoration in cases of shock, and that the changes were magically repaired by sleep. The production of sleep was the ideal treatment of shock and exhaustion.

Fatigue from want of sleep alone may give a shock-like condition, Crile (508, 553) found that experimentally want of sleep in rabbits produced histological changes in the brain, similar to those of traumatic shock.

Fatigue in the presence of shock markedly aggravates the condition. This was commonly observed in cases of Wound Shock in the Great War.

#### (b). PAIN.

This factor is not necessary to the production of shock, for general anaesthesia abolishes pain but not operative shock.

Violent stimulation of afferent nerves presumably acts in a similar manner to pain, i.e. by producing reflex effects on the circulation and respiration (see under TRAUMA and CENTRAL NERVOUS SYSTEM), and it has not yet been proved that this factor alone causes shock, as the animals have always been under anaesthesia. A disagreeable smell or sight may give a shock-like effect,

and more sensitive parts seem to give a more severe degree of shock, e.g. the finger, testicle, or larynx.

It is commonly believed, however, that pain aggravates shock. In Wound Shock, due, e.g., to fracture of the femur, pain from want of immobilisation and extension was believed to be an important aggravating factor, before the general introduction of the Thomas splint.

(c). LACK OF FOOD AND WATER.

Lack of food is well known to predispose markedly to traumatic shock. The general effect is to produce a general lowering of vitality of all the essential organs. Its aggravating influence is seen in cases of oesophageal obstruction, etc., but in these cases other factors, such as cancerous cachexia and toxæmia obscure the effects of pure starvation.

Lack of water undoubtedly influences the tendency to shock. The effect lies chiefly on the circulation. Presumably the blood volume is reduced, and so the tendency to circulatory failure is accentuated. In this connection, however, a large margin of safety probably exists, as Underhill and Kapsinow (608) suggested. They found that in dogs with increased concentration of blood from being deprived of water for a number of days, the blood did not show the usual increase of concentration after peptone or histamine injection. Probably the blood was already concentrated almost to its limit. In cases of shock, lack of water markedly aggravates the condition. Soldiers deprived of water in the Great War were found to suffer more severely from wound shock. Similarly, deprivation of water, violent purging,

etc., before operations, is supposed to favour the development of operative shock.

(d). DEBILITY.

Debility from antecedent illness or present constitutional disease, in particular the cachexia of malignant disease, markedly predisposes to shock. L. Mummery(31) emphasised that the pre-operative condition should exclude any such debility.

5. HAEMORRHAGE.

This is one of the most shock-producing factors. As it is, however, only sometimes present in cases of traumatic shock, and not always, like trauma, it is not an essential causal factor. If haemorrhage alone be present, then certain signs of shock appear. Especially if its extent be considerable, it may produce a shock-like condition which closely resembles true traumatic shock.

What are the shock-like effects?

The effects of haemorrhage resemble in general those of traumatic shock, though in some respects they differ (see Differential Diagnosis).

The clinical signs are similar, because both conditions depend on loss of circulating blood-volume. In both very little anaesthesia is required.

Central Nervous System. Nerve cell changes, apparently identical with those of traumatic shock, were observed by various workers, including Dolley(74)(97) and Crile (657).

The blood and circulation. The circulatory changes



are similar to those of shock and indicate circulatory failure. The pulse rate is always increased. The blood pressure falls rapidly, and greatly aggravates that due to traumatic shock. Using the method of artificial perfusion (see CIRCULATION—Supposed Dilatation of Arteries), Sollmann and Bilcher (143) found that haemorrhage progressively stimulated, depressed, and paralysed the vasoconstrictor centre. As shown by the perfusion flow, the centre was paralysed, when 35-40 ccs. per kilo. had been bled, and the blood pressure had fallen to 30 mms. Saline infusion before paralysis might restore it. The low blood pressure level depended on the amount of blood lost, not on the rapidity. Bayliss (311) found that in experimental traumatic shock, produced in various ways, haemorrhage even slight in degree, greatly aggravated the condition. Experimental bleeding of a cat of  $\frac{1}{4}$  of its blood was not dangerous, but, if other factors produced a fall of blood pressure then a much slighter haemorrhage gave a permanent fall of blood pressure (321). Similarly, if slight haemorrhage were repeated several times. Cannon (567) called this "critical further bleeding". Mann (502) and Cannon (567) found that the fall of arterial pressure was at first compensated, and then not recovered from. Similarly, if after one or two small haemorrhages, the abdominal viscera were exposed for a short time, again compensation did not occur. (502).

The volume of blood-flow, Gesell (368, 599) found, was diminished in haemorrhage, just as in traumatic shock. It was decreased out of all proportion to the decrease in blood volume. In slight haemorrhage, (10% decrease of

blood-volume), marked reduction of even 60% might occur along with a rise of blood pressure probably from central vasoconstriction compensating the concentration of blood which was noted. On stimulating the Chorda Tympani, he found the volume-flow was reduced out of all proportion to the reduction in mean blood pressure. Conversely, with injection of Gum Acacia (450,599). The "nutrient-flow" (i.e. vol. flow  $\times$  concentration of blood) might thus be increased several hundred per cent, because the volume-flow was increased out of proportion to the dilution. Decreases of "nutrient flow" might occur along with increased volume-flow and increased mean blood pressure.

The heart, as in traumatic shock, is not primarily affected. Meek and Eyster (369) found that heart output in the initial stage of a small haemorrhage in dogs remained constant, as determined by the diastolic heart size seen with the X-rays, until 2% of body-weight of blood was lost.

The reduced blood volume in effective circulation is one of the central features in both shock and haemorrhage, and explains the similarity in their clinical signs. Blood counts show a marked decrease of red corpuscles. They might be reduced to a million or less, and the Haemoglobin percentage in proportion, the minimum being reached 1-3 days after, according to Gulland and Goodall (115). The Total Haemoglobin Estimation, derived from the Haemoglobin percentage and blood volume gives a good indication of the patient's condition, according to Robertson (288) and Robertson and

and Bock(291).If it were twenty five per cent transfusion was indicated.

Fall of alkali reserve takes place.Gesell(450)found that,in experimental bleeding,as the blood volume diminished and the Haemoglobin percentage remained constant,the alkali reserve fell simultaneously.This indicated that the disturbances in oxidation varied directly with the decrease in volume of blood-flow.

Diminished tissue activity is indicated by several changes.The glandular secretions are diminished,as in shock.The secretion of urine and of saliva,as Bayliss (309)found,are rapidly decreased.Decreased response to stimulation in the muscles was observed in dogs by Gesell(600)while the converse occurred with injection of gum-saline,probably from increase in "nutrient-flow". Perhaps,too,the resistance to poisonous products of injured tissues is lowered,as in histamine shock,Dale (477)suggested.

The respiratory changes are similar to those in shock, hyperpnoea or dyspnoea being present.

CO<sub>2</sub> administration after haemorrhage gave a greater hyperpnoea,according to Gesell(606).Probably the reduced volume flow had diminished the transport of CO<sub>2</sub> in the blood(and also the rate of oxygen consumption). Conversely,after injection of gum acacia,probably from the increased "nutrient-flow"and consequent increased transport of oxygen,decreased reduction of oxyhaemoglobin, and decreased acid metabolites.

Decrease in oxygen after haemorrhage in unanaesthetised dogs was resisted just as before,in Gesell's experiments

(598). This was probably due to the diminished flow of blood and the weak stimulating power of lack of oxygen on the respiration.

#### HAEMORRHAGE-SHOCK.

If haemorrhage be absent, traumatic shock is sometimes absent. It is a common observation that, in surgical operations, in which loss of blood is carefully and thoroughly controlled, signs of shock either do not appear or do so in lessened degree.

Haemorrhage occurring in the presence of traumatic shock, on the other hand, greatly aggravates the condition. In Wound Shock it was generally present in some unknown degree. In fact, several observers suggested that it was the main cause of the condition, and in cases in which it had occurred to a moderate or serious degree, a special type was distinguished as "Haemorrhagic Shock." Similarly, in accidental wounds in civil life. In operative shock, too, the detrimental effects of loss of blood are well known to surgeons. Where severe shock is developing, even slight loss of blood may greatly aggravate the condition and a fatal result ensue. Mann (502) concluded that a combination of deep anaesthesia, operative trauma, and haemorrhage was the most common cause of operative shock.

#### 6. TOXAEMIA.

Toxaemia may be a cause of traumatic shock. The progressive stage of Delayed Shock probably results from this factor mainly (see BLOOD—Absorption of toxic substances).



Toxaemia in the presence of shock markedly aggravates the condition. In the case of Wound Shock, the toxaemia of infection had a markedly aggravating effect.

Anaerobic infections, e.g. gas gangrene infection of muscles, and mixed streptococcal infection, in particular, were often associated with it. So frequently was the association observed that a special type of shock, in which infection was a predominating factor, was distinguished as Toxic Shock or Septic Shock or Infectious Shock. In Operative Shock, too, any toxaemia before or after operation has a markedly deleterious effect.

Wright and Colebrook(301) found that acidosis was present in gas gangrene infection.

If the Blood Pressure were low in this infection, intravenous gum-saline, according to Bayliss(330), helped the patient to combat it.

## 7. ANAESTHESIA.

The presence of this factor in operations is what distinguishes Operative or Surgical Shock from other varieties of Traumatic Shock. It cannot be the cause of Traumatic Shock in general, as these other varieties of shock occur without its presence. In the case of Operative Shock, however, produced in surgical operations under general anaesthesia, it is a factor, the effects of which require consideration, and which may possibly be a causal factor in the condition.

### What are the possible shock-producing effects?

The pharmacological action of the general anaesthetics on the Central Nervous System in general is to produce a progressive descending paralysis, commencing

with the highest cerebral functions and passing downward and effecting the medullary centres last of all. The details of the action belong to pharmacology(see Cushny 174)).The sensory functions are affected before the motor, and it is probable that the anaesthetics first act on the first afferent synapse(174).

This view was confirmed by the work of Forbes and his coworkers(211,212,601).These observers concluded that ether blocked the synapses between the 1st and 2nd. neurones,at first partially,and then almost completely, A preliminary investigation(211)showed that ether did not abolish action-currents in nerve trunks subjected to direct stimulation.Even under ether deep enough to stop respiration and cause death,action-currents and contraction of the innervated muscle still took place. Therefore,nerve impulse and action-current were inseparable,and the action current was a safe criterion of the presence or absence of nerve impulse in connection with the action of ether.The afferent impulses were then tested in decerabrate cats with a string galvanometer(212,601).Stimulating electrodes were applied to a large afferent nerve.e.g.sciatic,and the disturbances set up in the neurones of the fillet was recorded with the string galvanometer,both without and with ether. The action-currents showed that light ether decreased the currents probably in the 2nd.neurones,(fillet). This decrease was probably due to blocking at the synapses between the 1st.and 2nd.neurones,the block in the remaining synapses being incomplete.With deeper etherisation,more diminution resulted,probably from

blocking at more synapses. With deep surgical anaesthesia, there was great reduction, almost abolition. Therefore very few impulses probably passed the block, and ether did protect the brain from afferent impulses. Mann(253) found that some of the medullary reflexes were not blocked, if very strong stimuli were used.

Cytolytic changes in the nerve cells of the brain, viz. hyperchromatism followed by chromatolysis, were described by Crile(125,153,512,516,525,559) as occurring in experimental traumatic shock under ether and chloroform. Under curare the changes were no greater than under ether. Under  $\text{NO}_2$  and  $\text{O}_2$  these changes did not occur to the same degree. Under approximately equal trauma, Crile(514,515) found that the fall of Blood Pressure was much less and the condition of the animal was better, and the brain-cell changes were only a  $1/3$  as great as under ether. Either anaesthetic alone without trauma did not give such great changes. Changes in temperature and in electrical conductivity corresponded to the histological changes.

It is most probable that these changes result secondarily from anoxaemia due to the failure of circulation. As ether is more depressive on the circulation than nitrous oxide, greater secondary changes are produced. Crile(153,158,561), however, concluded that ether and chloroform first acted on the efferent path, and supposed that, the afferent path being unbroken, sensory stimuli reached and modified the brain cells just as if no anaesthetic had been given. The brain cell changes were due apparently to the discharge of energy

in a futile effort to escape from the injury. Under light anaesthesia, vaguely purposeive movements took place as though efforts to escape from the injury. When these movements were abolished, he supposed that the pain impulses had exhausted the brain cells.

He(526)attributed the protective action of Nitrous Oxide to its interference with the use of oxygen by the brain cells.

#### Blood and circulation.

Heart. The anaesthetics ether and chloroform exert a gradual depressive influence on the heart muscle. Nitrous Oxide does not affect the heart directly, but only by lack of oxygen, according to Kemp(8) and Trew(651). (See also Cushny(174)). This depression and decrease of output of the heart under ether may produce the fall of blood pressure. Sudden heart failure may occur with chloroform, especially light chloroform anaesthesia.

Levy(128) attributed this to the onset of ventricular fibrillation. It indicated an abnormal irritability of the heart under  $\text{CHCl}_3$ , which generally occurred at the beginning or end of anaesthesia, or under excitement, strong sensory nerve stimulation, or adrenalin. In deep  $\text{CHCl}_3$  the respiration failed first. These results were confirmed by Y. Henderson(150). The latter found that ether did not produce it, except in rare cases in which he attributed the result to acapnia. Cattell(484, 504, 654) showed that in experiments on heart volume of intact cats, ether decreased the output from the start, thus giving the fall of blood pressure. Large doses of adrenin intravenously counteracted the action of ether for an hour or more, probably from its action on the



heart, but pituitrin had no effect.

Blood Pressure. In its pharmacological action,  $\text{CHCl}_3$  produces a fall of blood pressure mainly by its action on the heart, and in a less degree due to the dilatation of the vessels of the abdomen. In ether anaesthesia the direct vascular action is opposed by the vasoconstrictor centre which is stimulated by the partial asphyxia.

L. Mummery (31) noticed that shock developed more after  $\text{CHCl}_3$  than after ether. In Wound Shock cases operated on under ether, Cannon (223, 226, 339, 342, 438, 567) and Cattell (484, 654) found the blood pressure was markedly reduced.

It might fall 30-40 mms. Hg. If other causal factors were present, e.g. cold, haemorrhage, infection, administration of the general anaesthetic might give a fatal result.

Impure ether alone, Mann (253, 347, 376) found, always produced a fall of blood pressure in 1 or 2 hrs. Low ether tension for many hrs. gave no lowering of blood pressure, but high tension gave a marked fall (253). With strong ether alone in animals, Cattell (484, 504, 654) found that the arterial pressure dropped suddenly, then recovered gradually. But in shocked animals there was no recovery and the blood pressure fell to zero. Peripheral vasoconstriction was caused by ether in intact animals and this compensated the decreased output of the heart.

But in shock it was absent, and pressor effects were diminished or absent. This fall of blood pressure under ether might be due to depression of the vasoconstrictor centre, or to an already existing maximal tone of the centre, so that there could be no compensation. Webster (129) found that in light ether anaesthesia, incision

of the abdominal wall might produce a fall of blood pressure, but Rich(588) found that preliminary light ether had a striking protective effect against traumatic shock, but once the blood pressure fell ether hastened shock. Animals kept under for one hour before the abdomen was opened were very resistant to shock from intestinal manipulation. If manipulation were begun immediately after anaesthesia, shock developed soon. Nitrous Oxide, on the other hand, had no effect on the blood pressure, Kemp(8) found, unless asphyxia were present. And this result was confirmed by Marshall(244) in wound shock cases operated on under  $\text{NO}_2$  and  $\text{O}_2$ , and by Cattell(484, 504, 654), and by Trew(651).

The blood volume. In Wound Shock cases under ether, Bassett(289) found that the haemoglobin readings indicated a dilution of the blood, followed by a concentration, and Dale's work(402, 403) indicated that the capillary walls became more permeable and so the blood volume, as found by Keith(408), became reduced. These changes did not take place under  $\text{NO}_2$  and  $\text{O}_2$ , or only slightly, including reduction in blood catalase, according to Trew(651).

Fall of blood alkali occurs during anaesthesia, Increase of H-ion concentration was found by Crile and Menten(194, 525) in normal men and animals with all the inhalation anaesthetics, ether,  $\text{CHCl}_3$ , and  $\text{NO}_2$ , both during and for about an hour after. Changes indicating this condition appeared both in the blood and urine. Austin and Jonas(262) found a reduction of 2-20 vols. % after ether anaesthesia proportional to the duration. It was

maximal at the close, and remained for about 5 hrs.. In average operation cases, Caldwell and Cleveland (274) found the degree of fall in blood alkali was negligible, nor did it vary much with the different anaesthetics, and so had no bearing on the choice of anaesthetic. No signs after operation were due to it. In etherised animals, Y. Henderson, Prince, and Haggard (254) found that fall in alkali reserve was at <sup>first</sup> sharp then gradual. During the first hour of ether, hyperpnoea was present and fall of  $\text{CO}_2$  content of arterial blood,  $\text{CO}_2$  capacity of blood, and  $\text{CO}_2$  content of alveolar air took place sharply, then more gradually. After the production of shock by manipulation of the intestines, little difference was observed. The ether hyperpnoea was regarded as primary, the fall of  $\text{CO}_2$  combining power of the blood secondary, i.e. the loss of  $\text{CO}_2$  controlled the alkali. The acapnial process was thus the converse of acidosis. Henderson and Haggard (361) concluded that under ether the  $\text{CO}_2$  capacity of the blood (alkali reserve) followed and was controlled by the  $\text{CO}_2$  content, and the  $\text{CO}_2$  content in turn was dependent on the alveolar  $\text{CO}_2$ , which was determined by the breathing. Ether hyperpnoea gave a very great reduction, but if there were no increase in respiration, only a slight reduction. If light ether combined with administration of  $\text{CO}_2$  maintained the alveolar air at normal level, no reduction occurred. Raymond (493) found the fall in alkali reserve in dogs under ether occurred gradually as etherisation was prolonged, and after 4 hrs. a rapid decline set in. It ranged from an average of 43 vols. % to an average of 34 vols. %,  $\frac{3}{4}$ -2 hrs. later fell

to 28 vols.%, and after 2-4 hrs. to 26 vols.%. Crile (655) found a fall from 46-32 % in dogs under ether. Reimann (465) obtained a fall of blood alkali after ether,  $\text{CHCl}_3$ ,  $\text{NO}_2$ , and stovaine, only in 15-20 % of cases.

Still more does this change occur if traumatic shock be present. In operations on Wound Shock cases under ether, Cannon (223, 339) found a marked decrease, even if of short duration. The fall was greater the less the margin of safety in the individual, and in severe cases an ominous fall occurred. It was greater under ether than under  $\text{NO}_2$  and  $\text{O}_2$ .

The Red Corpuscles probably tend to be dissolved by  $\text{CHCl}_3$  and ether, according to Cusny (174). In the blood  $\text{CHCl}_3$  is carried by the red cells for the most part and in the lecithin and cholesterin, and Buckmaster and Gardner (41) showed that the  $\text{CHCl}_3$  content of the blood rose very rapidly to a maximum, and might paralyse the respiratory centre. Subsequently a rapid fall took place, followed by a rapid rise to a maximum which was maintained. The rate of elimination was much less rapid than the intake. They also showed (85) that the chief respiratory danger was due to a direct interference with the oxygen-carrying function of the red cells. The dark colour of the blood was due to a diminution in the reduction of oxyhaemoglobin and ~~not~~ to a diminished ventilation, because the rate and depth of the respirations were not diminished. In Nitrous Oxide anaesthesia, no spectroscopic change was produced in the blood, Kemp (8) found. Leucocytosis occurs after ether but not after  $\text{CHCl}_3$ , according to Gulland and Goodall (117).



The Respiration under  $\text{NO}_2$  and  $\text{O}_2$ , Trew(651) found, was stimulated to 30 per min., then depressed.

Y. Henderson(91, 92, 95) concluded the painful afferent stimuli and light anaesthesia gave hyperpnoea, acapnia, and perhaps fatal apnoea vera, unless  $\text{CO}_2$  were administered. Morphin and full anaesthesia by diminishing pain hyperpnoea prevented acapnia and shock. Apnoea, he(92) pointed out, depended on the relation between the threshold of the centre for  $\text{CO}_2$  and the  $\text{CO}_2$  content of the blood and tissues. The sensitiveness of the centre to  $\text{CO}_2$  was diminished by deep anaesthesia and by morphin, i.e. the threshold was raised. Light anaesthesia, on the other hand, prevented apnoea.

Mann(253, 347, 376) suggested that reflex inhibition of respiration might play a part under deep ether. He showed that sudden death, which might be attributed to shock, might be produced under deep ether.

The  $\text{CO}_2$  in the arterial blood, Kemp(8) found, was greatly diminished in Nitrous Oxide anaesthesia.

The Adrenals were probably first excited, and later depressed by the anaesthesia. Elliot(105) showed that, under anaesthesia by ether,  $\text{CHCl}_3$ , and urethane, loss of adrenin content of the glands resulted.

#### Does General Anaesthesia Cause Operative Shock?

In brief, general anaesthesia depresses the circulation respiration and muscle-tone centres, and consequently decreases tissue oxidation. The hyperpnoea and asphyxia associated with its administration are also important, especially if the blood be not returning completely to the Right heart.

In the first place, certain fallacies, as Mann (253) pointed out, must be considered. Other factors that may produce signs of shock require to be excluded (see Causal Factors). Haemorrhage may be present, the patient may react to it readily, and the amount is uncertain. Trauma of viscera may produce loss circulating blood in the traumatised areas, mainly from the local peripheral mechanism. Excessive nerve stimulation, as a shock-producing factor is still sub judice. Pulmonary fat embolism in fractures and in operations involving trauma to much fat is a possible factor.

(1). General anaesthesia alone may cause a shock-like condition, and it may be difficult to judge after a long operation how much the effects are due to the operative trauma and how much to the anaesthesia. The effects under Nitrous Oxide and Oxygen are much less in general than those under Ether and Chloroform. The former has little depressant effect on the circulation. The fall of blood pressure under ether, due partly to action on the heart, partly to depression of the vasoconstrictor centre is more easily recoverable from than when traumatic shock is also present. The compensating action of the V.C. centre is still present and effective, whereas in shock, the mechanism, which has been acting at the maximum, becomes more severely damaged secondarily by the failing circulation.

(2). General anaesthesia in the presence of shock, it is well known, aggravates shock. Nitrous Oxide and Oxygen, however, is much the least injurious of all the anaesthetics. With Ether and Chloroform, the progressive

fall of Blood Pressure in particular is aggravated, as the vasoconstrictor centre is probably still further damaged and unable to compensate. The oxygen supply to the tissues is still further lessened from the increasing failure of the circulation. In addition, the resistance to toxæmia from the injured tissues is probably depressed, as Dale (477) suggested, more under Chloroform and Ether than under Nitrous Oxide and Oxygen.

## SECTION V. DIFFERENTIAL DIAGNOSIS.

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The diagnosis of Traumatic Shock is usually easy. If pure and uncomplicated, and observed within 24 hrs. of injury, Wound Shock presented a picture the signs of which were pathognomonic. (1). Sometimes, however, where several causal factors were present, it might be difficult to judge how much of the effects were due to each separate factor. In other cases the condition might not really be due to the trauma, and therefore not be Wound Shock, but be due entirely to other factors. Similarly with shock due to accidental injuries and with Operative Shock. (2). Other forms of Shock besides Traumatic Shock might closely resemble it. (3). Other conditions that were not shock might resemble it.

### (1). CAUSAL FACTORS OF TRAUMATIC SHOCK.

Each of the possible causal factors (see SECTION IV.) present in each individual case must be allowed for.

#### HAEMORRHAGE.

In exceptional cases it is practically impossible to distinguish between haemorrhage and shock. The differences seem to depend more on the sequence than on the nature of the processes. Haemorrhage, however, is now regarded more as a form of asphyxia, the essential element being a loss of corpuscles, not of plasma. (See Crile (81) and Gesell (450)).

A consideration of the HISTORY might suffice to exclude or suggest haemorrhage. Care and patience may be needed, as Bernheim (276) pointed out, to obtain an



accurate history.

The CLINICAL SIGNS though similar generally differ in several respects. The haemorrhage itself is usually evident. A preliminary stage of excitement occurs in haemorrhage. The patient is usually anxious and restless, whereas in shock he is inclined to be apathetic and listless (See Crile (81)). Extreme pallor occurs in haemorrhage, cyanosis in shock. Bernheim (276) described the facies as "cadaverously cyanotic" in haemorrhage. The breathing is rapid and shallow and "air-hunger" may be present.

The PULSE is always increased in rate. Crile (81) and Polak (391) emphasised. It is small and weak and slightly irregular.

BLOOD PRESSURE. Owing to the more rapid loss of blood the B.P. falls from the first, though compensatory vasoconstriction takes place in the empty vessels. Malcolm (579, 582) suggested that this contraction of the vessels was passive in haemorrhage, active in shock. A falling diastolic arterial pressure, according to Wiggers (336), is suggestive of haemorrhage. Diminishing pulse-pressure was emphasised by Polak (391). This sign and increasing leucocytosis might be present, while the red-count and Haemoglobin % showed little change. A low venous pressure also, as Wiggers (336) observed, comes on early. It may be measured by von Recklinghausen's method: with one hand placed on the patient's thigh, the other on the bed, if the latter remain empty, the pressure is low. The falling diastolic arterial pressure, the early low venous pressure, and the fall in the red-count and

Haemoglobin %, Wiggers (336) suggested, were the differential factors.

REDUCED BLOOD VOLUME. The loss of blood volume in haemorrhage is rapidly followed by regeneration. Lymph passes rapidly from the tissues into the empty vessels and the blood is diluted, possibly because, Keith (410) suggested, the pressure in the tissues is higher than in the vessels, though Leonard Hill (61) denied that this was so. The rate of recovery of blood volume, Keith found, was much more rapid than in shock. The mechanism for controlling the blood volume is thus able to compensate partially in haemorrhage, but in Traumatic Shock it is greatly impaired. Robertson and Bock (291) found that the reduced blood volume might be largely counteracted by giving a large fluid intake. Red counts show a decreased number of reds; in shock and increased number. The Haemoglobin % is low; in shock, high. Compared with the red count, the Haemoglobin % readings are relatively low, and the colour index is therefore below unity. In shock, the colour index equals 1. In moderate haemorrhage and shock the colour index may be equal to .65-.7. A low Haemoglobin % reading, therefore, suggests haemorrhage in shock cases. Bainbridge and Bullen (239) pointed out that in shock-haemorrhage the Hb. % is the resultant of two different processes. Shock tended to concentrate the blood, haemorrhage to dilute it. If low, it indicated that the increase in blood volume was taking place at the expense of the tissue fluids and the patient might recover. If approximately normal, the physiological reaction to loss of blood was being counteracted by the tendency of shock to concentrate the blood, and

the patient might die. Single blood examinations were, according to Bernheim(276), of little use, because, the vascular system was compensating. Sometimes, however, a definite drop might be shown by one examination. A series of readings was of more value. During regeneration and recovery, the red-count rose and microcytes appeared in the circulation. Leucocytosis was observed by Crile (82) in 1909 and this was confirmed by various observers including Harrison(348) and Polak(391). Increase of blood platelets also occurred, according to Gulland and Goodall (115). The coagulation time of the blood is diminished, i.e. the coagulation power is increased, as the blood is lost, according to Crile(77) and Gulland and Goodall (115). In shock no change occurred according to Crile (80). Restoration of blood volume by saline was useful in haemorrhage, but useless in shock.

CAPILLARY STASIS. is not present in haemorrhage as it is in traumatic shock. The capillary red count was relatively much lower than that of shock alone, the venous red count considerably lower. On the contrary, constriction of the small venules and capillaries was seen microscopically by Meek and Eyster(541). This was probably an effort to keep up an effective circulation. The decreased viscosity of the blood, Gesell(368) suggested, tended to counteract the circulatory failure, whereas in shock the increased viscosity augmented it.

THE REACTION OF THE BLOOD is not changed so much as in traumatic shock, according to Crile(657)

THE BASAL METABOLISM, Aub(497) found, did not show any constant changes in haemorrhage as it did in shock.

TOXAEMIA.

Acute streptococcal infection after operations may seem identical with shock, as Bernheim(276) described. Toxaemia from gas gangrene or acute streptococcal infection often closely resembled Delayed Wound Shock. It was distinguished, however, by the local condition of the wound, and its time of onset, viz 2nd. to 4th. day. Sometimes, however, signs of gas gangrene were present within 12 hrs. (See Quénu (397), and Guyot and Jeanneney (569)). A rise of blood pressure sometimes indicated the onset, as observed by Drummond and Taylor(290), but was associated with increasing pulse rate and deterioration in general condition. Toxaemia from intestinal paralysis and absorption of toxins after abdominal operations might simulate Operative Shock, as Rendle Short(425) pointed out.

(2). OTHER FORMS OF SHOCK.

Anaphylaxis after Anti-tetanic Serum injection might resemble Wound Shock, the signs of the former being dyspnoea, fall of blood pressure, vomiting and other gastro-intestinal disturbances, accompanied by collapse and sometimes convulsions. Signs of urticaria and oedema, however, differentiated it.

(3). OTHER CONDITIONS THAT MAY SIMULATE SHOCK.SYNCOPE.

Cases of failure of heart compensation identical in signs with shock were described by Bernheim(276). Syncope, however, results from mental effects more often than shock, and is supposed to be caused by a sudden anaemia of the brain due to weakening or arrest of



the heart's action. It is more rapid in the onset and more transient, and recovery is rapid. An all-powerful stimulus is supposed to neutralise all other afferent stimuli, and cause sudden relaxation of vascular and muscular tone, with consequent defective return of venous blood to the Right Heart and cerebral anaemia (See L. Hill(63), and Guthrie(349)). According to Henderson(373), in syncope there is dilatation of the arteries and decreased peripheral resistance, but in shock a decreased venous return.

#### COLLAPSE.

Collapse appears to be identical with Secondary Shock, in some cases. The causal conditions, however, might be different. Trauma need not be present, and in the case of Asiatic Cholera loss of fluids is the essential causal factor, and fluid escapes from the blood into the tissues. Severe diarrhoea and vomiting may be present. The features are shrunken. The nervous system is not primarily affected. The blood may be very concentrated and viscid, even like tar. The organs are tough and leathery and of high specific Gravity. Unlike shock, treatment by stimulants may be successful. Cowell(416) suggested that collapse only differed from shock in time relationship, being more insidious and slower, in its development.

#### OTHER CONDITIONS.

Commotional Shock or true "Shell Shock" is a condition quite different from Traumatic Shock. It is probably due to sudden compression and decompression of air from a violent explosion. Sometimes actual

concussion, from violent contact with solid materials such as sandbags, might play a part, according to Mott (431, 434). Mott (430) also thought that carbon monoxide poisoning from the gas generated by the explosion was more common than was generally supposed. Consequent on this vibration of the air, were found organic changes in the brain and spinal cord. A low blood pressure, however, might be found according to Porter (210) in cases of "Shell Shock" with paralysis. Concussion of the brain from head injuries, spinal cord injuries, e.g. fracture-dislocation of the spine with crushing of the spinal cord, which resembles "spinal shock" experimentally produced in animals by transection of the spinal cord, as Pike (121) pointed out, crushing of the thorax or abdomen without significant internal injury, etc. all differ considerably from traumatic shock. Cerebral Haemorrhage, Thrombosis, and Embolism, Delirium Tremens, and Chloroform Asphyxia, may sometimes resemble shock, but in most cases are widely different. In operations, Chloroform Asphyxia comes on suddenly, Operative Shock gradually. The signs are similar, but the effect of treatment, e.g. lowering the head, etc. quickly differentiates them.

Fat Embolism came on later than Immediate Shock. The dyspnoea was greater, and might be accompanied by bloody foam from the mouth or haemoptysis; rales in the chest; oil globules might be present in the urine; and the temperature, though generally low, often fluctuated. The pressure in the pulmonary artery and right ventricle was rather high, but in shock, according to

Wiggers(336), it was low. Meltzer(36) pointed out that von Recklinghausen's test for venous pressure helped to differentiate them.

"Spinal Shock" resembles Traumatic Shock in the particular of loss of muscle tone. The cerebral anaemia from the lowered blood pressure due to section of the upper thoracic spinal cord, moreover, might damage the brain functions, according to Pike and Coombs(251). In many respects, on the other hand, they are different. Their causes are different, "Spinal Shock" being due to experimental section of the lower cervical spinal cord, though similar phenomena may also be produced, without section of the spinal cord, by experimental cerebral anaemia, as Pike and his coworkers have shown. The phenomena are also different in many ways. Those of "Spinal Shock" include depression of all the nervous functions below the section, severe fall of arterial pressure, and loss of vasoconstrictor reflexes. Vigorous animals usually recovered after a time, according to Sherrington(481), and exhibited reflex movements and pressor spinal reflexes. He found that the time varied with the animal, being some hours in the case of the frog, days to weeks in the dog and cat, and still longer in the monkey, in which, as in man, the "shock" was more intense and long-lasting. Again, the splanchnic vessels were dilated and the viscera congested, and with exposure this congestion increased. If the anaesthesia were withdrawn, response to stimulation returned. Intravenous injection of gum saline, according to Bayliss(326), had only a transitory effect.

SECTION VI. CLINICAL SIGNS.

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In Wound Shock and shock from accidental injuries, two types may be distinguished, viz. Immediate and Delayed. (See Cowell(224)). Surgical or Operative Shock generally conforms to the Delayed type. Immediate Shock, which was relatively rare in the Great War, appears immediately on receipt of a very serious injury. The blood pressure shows a marked and progressive fall. According to the severity of the condition, one of several results may follow, viz. (a) death in severe cases; (b) reaction with gradual rise of blood pressure to the normal level and recovery; (c) after a short interval, fall of B.P. again and development of Delayed Shock. Delayed Shock comes on after an interval of several hours from the time of receipt of a moderately severe injury. The blood pressure may at first be unaltered, or slightly increased with the excitement due to the injury, depending on the temperament; then after an interval it progressively falls; or the condition may follow Immediate Shock after an interval. Gradual recovery or death may result.

British observers called these types "Primary" and "Secondary" respectively. (See Cowell(224)). French observers, including Lacoste and Quénu(392) and Quénu, Duval, and Mocquot(637, 640), however, in addition to these types, also distinguished Secondary Shock, which was the result of, not only the trauma of the wound, but also





of septic infection, etc. They also described a type called "mitigated shock".

### EARLY SIGNS.

These are very important to recognise quickly, in order that the condition may be prevented from developing. The pulse, facies, and other signs collectively indicate the onset of the condition. The pulse may show an increasing rate, perhaps of 20-30 beats per min., and this change, if associated with other signs, e.g. marked pallor or coldness of body surface, indicated the onset of shock, according to Kelly (11). Malcolm (582) repeatedly emphasised, however, that at first the pulse did not increase in rate, and might become larger and of higher tension. Then it might slow in rate and diminish in size and force until imperceptible, while the carotids pulsated strongly and the heart-sounds were loud and clear. These signs indicated that the heart muscle was responding well, and that the arteries were contracted. Then, as shock developed, the pulse increased in rate and became imperceptible, the carotid pulsation became smaller and weaker, and the arterial pressure fell.

The Arterial Blood Pressure probably changes only after Delayed Shock has existed for some time. At first it is maintained probably by extra activity of the vasoconstrictor centre causing greater contraction of the peripheral vessels. Later the blood pressure begins to fall, probably as the effect of loss of blood volume overbalances that due to the vasoconstriction. A low B.P. by itself does not necessarily indicate shock, however. Other signs must also be present.

Other early signs may be associated with these changes.

The facies may show a marked pallor, the body surface may be cold and clammy, with fall of temperature and profuse perspiration. In operations, the tissues may be blanched and don't bleed, or slow recovery from the anaesthetic may be suggestive, according to Kelly(11)

Various tests before operation may be carried out. Polak(309) laid stress on the importance of the pulse-pressure and renal function tests. If both were low, the latter, say 20-30%, instead of the normal 60% phthalein output for 2 hrs., the patient was a "bad risk". During anaesthesia, the pulse pressure was taken at the close, 6 hrs., and 24hrs. after, and in shock cases every hour till reaction set in; the pulse rate for the first 6 hrs. after; blood count and Haemoglobin % estimation were done; and the phthalein output estimated 6 hrs. after.

Judgement as to the relative importance of the causal factors is also required, in order that the appropriate treatment may be carried out. In Operative Shock such factors as haemorrhage, crushing of tissue, septic infection, etc. may require to be excluded.

#### SIGNS OF ESTABLISHED SHOCK.

The patient is in a state of general prostration, and seems indifferent to his surroundings. He answers questions correctly, showing that his intelligence is unimpaired, and complains of thirst, as his mouth is parched. Vomiting may take place and increase the thirst. He feels chilled and may shiver. Pallor of the skin and general perspiration are present, the skin

being cold and clammy to palpation, and even the breath is cold. In the Delayed stage of Wound Shock, this pallor was accompanied by cyanosis, particularly marked in the extremities and finger-nails. The muscles are weak and flaccid. The sphincters are usually relaxed with incontinence of urine and faeces, according to Howard (461), or retention may be present. Sensibility to pain is diminished. The expression is generally apathetic, perhaps with wrinkling of the forehead indicating anxiety; or it may be drawn and haggard, with sunken eyes and hollow cheeks, and dilated pupils, which, however, react to light. The conjunctival reflex is present. The Pulse progressively increases in rate, and diminishes in strength, volume, and tension, until it is imperceptible. The blood pressure progressively falls. The body temperature also progressively falls to 96 deg. Fah. or lower. The rectal temperature, however, according to Howard (641), may be raised in Immediate Shock. The respiration is slow or rapid, and shallow, and may be irregular and sighing. The knee jerks are generally elicited, but may be absent in severe cases. The urine is reduced in amount.

Reaction may be set in in a few hours and recovery take place. Vomiting often ushers it in. He begins to take notice of his surroundings, his colour improves, the skin becomes warmer, the pulse stronger and fuller, respiration slower, more regular and deeper, and the temperature rises to 100 deg. F. or more.

Death, on the other hand, may supervene rapidly, or more gradually. It may take place quietly or with great restlessness and dyspnoea. Consciousness remains to the end, though anxiety may change to mental dulness and

lessened sensibility.

These features were well shown by the cases of Wound Shock in the Great War. Predisposing conditions were present, viz. exposure to cold and wet, lack of water, want of sleep, mental strain, or extreme exertion, together with haemorrhage, pain or disturbance. Later gas gangrene infection might greatly aggravate the shock. Owing to these associated factors, the features due to the shock itself were apt to be obscured, while the part played by each individual factor could only be judged with difficulty.

(See 218, 286, 333, 334, 353, 480, 535, 224 (or 340), 225 (or 341), 226 (or 342)).

#### ILLUSTRATIVE CASE OF IMMEDIATE SHOCK:

Capt. C., died of wounds, on 28th., Sept., 1915, at the Battle of Loos—death from severe immediate shock in about  $\frac{1}{2}$  hr.

Of sensitive temperament, he had heavy responsibility during the first four days of the battle, being in command of the battalion of 2nd. R.S.F.A. destructive bombardment of the captured German trench by 4.2 in. and 5.9 in. (several batteries) was in progress and was battering the trench in. One of these high-explosive shell-bursts made a "direct hit" on the trench, striking Capt. C., killing two of his companion officers, and wounding a third. I saw him 10-15 mins. after receipt of his wounds.

He was suffering from multiple wounds of the head, body, and limbs, all of slight or moderate severity, none serious individually, no bones or internal cavities being implicated, and there being no great loss of blood.



He was lying helpless in the battered-in trench, his clothes torn in pieces by the shell fragments, and soiled with the dried earth and dust from the explosion. He was lifted into an adjacent trench-shelter, and covered with some clothing, while the severe bombardment continued.

Conscious but stunned, he was too ill to speak, except in a forced whisper. His face was pale, with an anxious expression. His jaws were clenched and his teeth crunching together, so that an attempt to force down some brandy was found impossible. His hands were clenched, and his body surface cold.

His respiration was panting, like "air-hunger", very rapid and short, with no pause between inspiration and expiration, mouth open, and the accessory and extra-ordinary muscles of respiration acting. His pulse was rapid and weak, then became imperceptible. The blood pressure estimated by the finger was low. He was very restless at first, but became quiet and rapidly weaker, and died in about  $\frac{1}{2}$  hr. The outstanding clinical sign seemed to be the type of respiration, so much so that one instinctively fanned his face.

(See APPENDIX A for other selected cases.)

SECTION VII. EXPERIMENTAL TRAUMATIC SHOCK.

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It is doubtful whether experimental traumatic shock is the same as the clinical condition. The former applies to healthy animals, the latter to human beings whose vitality may be more or less depressed by various conditions that predispose to shock. In experiments on animals, it is very difficult to reproduce the environment that obtains in the conditions in man, and Mann(347) believed that only a few of the experiments approached the clinical condition.

In the production of experimental traumatic shock, the primary causal factor may vary, and hence, as Mann (347) pointed out, contradictory conclusions were arrived at by different investigators. In every case, however, the cause of death was a failure of compensation of some sort. As in the clinical condition, so in the experimental, two types were described by Guthrie(255). viz. (1) the one with immediate onset on receipt of the active agent; (2) the other in which the onset occurred some time later. Raymond(493), taking as the basis the length of time of survival after the trauma, differentiated four types. These ranged from the more severe with sudden onset and death, through the usual two intermediate types, to the mild with few or no cardinal signs of shock.

THE STANDARD.

A standard as to what is meant by shock requires to be defined in these experiments. For many of the earlier

observers, including Crile(12) and Mummery(30), fall of arterial pressure, rapid pulse, and respiration constituted the index. But it is well known now that anaesthesia alone may cause these changes. Meltzer(55) early emphasised <sup>that</sup> the general mental state, and the state of sensibility and motility, as well as the condition of the cardio-vascular and respiratory functions must be considered. In particular, he pointed out that low blood pressure was not the only, nor even an essential, sign. Mann(142,195) proposed later that the following signs should be present, viz.: loss of sensibility, pallor of mucous membranes, small weak pulse, markedly lowered blood pressure to  $\frac{1}{2}$  or  $\frac{1}{4}$  of its original level, and irregular, rapid, shallow, or gasping respiration. At the same time, no haemorrhage should be allowed to occur. Fall of arterial pressure down to 50 mms. of mercury was chosen as the "critical level" by Porter(210), because, after falling to this level, it was difficult to restore it to the normal for any time. According to Guthrie(255), a reliable index was furnished by the occurrence of a markedly prolonged inspiratory pause. The requirement that functional changes in the Central Nervous System, e.g. apathy, reduced sensibility, loss of reflexes, etc., should be present was emphasised by Wiggers(372). He held that traumatic shock was present if, after prolonged ether, the animal, instead of recovering in the usual 15 mins., lay relaxed for hours and failed to respond to sensory stimulation. He also found that a normal blood pressure might be present and yet the circulation might be serious, as indicated in the

optical arterial pressure curves by decline of pressure in systole only, and slight or no decline in diastole. Gesell(450) also found it indicated by a reduced volume of blood flow. Nevertheless, a progressive fall of blood pressure to the shock level is a reliable sign. A progressive fall of B.P. to 50 mms. of mercury. Erlanger (257,454) found was generally irreversible, and this is therefore generally taken as the shock level, but the other signs are noted.

#### METHODS of producing EXPERIMENTAL TRAUMATIC SHOCK.

The animals, generally dogs, are under light and uniform ether anaesthesia.

1. Stimulation of afferent nerves. This method appears to be effective only sometimes in producing Traumatic Shock. Moreover it is much more difficult to bring on shock in this way than by other more effective methods. Most experimenters accordingly resorted to exposure or manipulation of abdominal viscera, amputations of limbs, etc. In order that shock may be produced in this way, it appears necessary that the stimulation should be prolonged for many hours, but under these circumstances other factors enter into play. (See CENTRAL NERVOUS SYSTEM, and Causal Factors).

2. Exposure of the Abdominal Cavity. This method is one of the most effective in the production of experimental traumatic shock. If sufficiently prolonged it always produces signs of shock. It seems to approach most nearly to shock in abdominal operations. Before the experiment the animal may be fasted for 12-18 hrs. It is then etherised, incubated at a uniform temperature,



and constant surgical anaesthesia maintained. The abdomen is opened, and the viscera exposed and manipulated. Mann (447,459) found that gentle handling continued for 15 mins., followed by replacement of viscera and closure of the abdomen always produced shock. Or sponging with dry gauze might be used. Or the animal might be changed from one side of the body to the other. Wiggers (336), after exposing the intestines, passed a stream of warm moist air over them without any manipulation. After the blood pressure had fallen, and remained stationary at the shock level, generally 50 mms, after 1 or 2 hrs., the viscera were replaced and the abdomen closed. Erlanger (257) found that after 2-5 hrs. the arterial pressure might be 50 mms. Hg. Raymond (493) used gentle and continuous manipulation of the intestines for 15 mins., followed by closure of the abdomen. If the arterial pressure was not lowered, the process was repeated after an interval, several times if necessary. Or traction was exerted on the kidney or trauma applied to the liver or urinary bladder. He then inflated the entire gut with warm moist air to a pressure above systolic for 10 mins. to abolish the circulation in the gut, and cause asphyxia of the vascular and intestinal muscle. Several factors may enter into the causation of shock produced by this method. Nerve irritation (see CENTRAL NERVOUS SYSTEM), circulatory changes (see Circulation) loss of  $CO_2$  (see Respiration), etc.

### 3. CRUSHING OF MUSCLE.

This method is one of the most effective in giving experimental traumatic shock. Turck (445) early practised this method, and his results were confirmed by Bayliss

The flexor muscles of the thigh were traumatised by a hammer in anaesthetised cats without breaking the skin, but causing rupture and bruising of the muscles. The cause of the shock in these cases was proved to be toxic absorption. (See BLOOD—Absorption of Toxic Substances.).

#### 4. OTHER METHODS.

In the following methods, the group of antecedent conditions does not closely correspond to that obtaining in shock, though the resulting conditions are more or less analogous to it.

##### (a). INTRAVENOUS INJECTION OF HISTAMINE--"HISTAMINE SHOCK"

The toxic action of Histamine was investigated particularly by Dale(304,402) and his associates. By the intravenous injection of relatively large doses in anaesthetised cats and dogs, "Histamine Shock" was produced. This condition was characterised by fall of blood pressure, associated with, and probably caused by, paralytic dilatation of the capillaries, emptying of the veins and heart-chambers, all leading to circulatory failure and acute oligæmia. In the local and general effects, Histamine resembles many other substances not related to it, and including various bacterial poisons. In the production of Delayed Wound Shock, in which a prominent feature was oligæmia, absorption of aseptic toxic products from injured tissues was believed to play a part, and therefore the two conditions were supposed to be analogous. It was, moreover, just possible, though Dale did not claim it, that histamine might be formed

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from histidine, an amino-acid, which might be produced in the hydrolysis of proteins of liver and muscles when the tissue was injured. (402, 403).

The action of Histamine locally applied to slightly scarified skin was to produce the phenomena of inflammation. It stimulated the tone of the plain muscle throughout the body. In particular, the tone of the arterial muscle was increased, e.g. arteries of the lungs, heart, etc. Similarly, intestinal muscle, giving rapid peristalsis. Similarly, spasm of the bronchial muscle. If, therefore, the blood-vessels were perfused artificially, the arteries contracted. On the other hand, it relaxed the tone of the capillaries throughout the body by poisoning their endothelium. For in certain animals, e.g. the carnivora, monkeys, and probably man, intravenous injections of smaller doses, Dale and Richards (304) found, gave a fall of arterial pressure. This was due, not to any diminished output of blood from the heart, or obstruction of blood-flow through the liver, but to peripheral vasodilatation. That the nervous mechanism was not responsible was demonstrated by an experiment in which, after all the nerves of a limb were cut and allowed to degenerate completely the dilatation from Histamine was intensified; whereas, if the denervated limb were perfused, the same vasoconstriction resulted. Then if a suspension of R.B.C.s or hirudinised blood (to supply oxygen) and epinephrin were both added to the perfusing fluid, the vasodilatation was antagonised and the usual vasoconstriction appeared. The action must therefore be due to poisoning of the capillary endothelium, according to Dale and Richards (304).

With larger doses, 1-2 mgrms. per kilo, injected intravenously in anaesthetised cats, "Histamine Shock" was produced. (See Dale, Laidlaw, and Richards (402), Dale (86), 99, 306). The arterial pressure showed three phases: (1) fall to 50-60 mms. Hg., associated with constriction of the pulmonary arteries and over-dilatation of the Right heart, and lasting a few secs; (2) arrest of the fall or rise to the original level, with constriction of the systemic arteries, of 30 secs. duration; (3) steady fall to 30-50 mms. Hg. in 4-10 mins., with rapid decline in the output from the heart. A slow infusion gave a prompt fall, then steady decline, with no recovery. On inspection, the heart and arteries were almost empty, the great veins only partly filled, and the portal vein flat. The liver and spleen were pale, but transparent tissues like the bowels showed the dusky flush of capillary congestion, and networks of venules filled with dark blood. The capillaries throughout the body were fully dilated, having lost their normal tone, so that the blood percolated into their network of channels as into a sponge; these vessels had been shown to be able to <sup>hold</sup> 750 times their normal amount of blood. Consequent on and associated with this dilatation, the blood-flow was greatly retarded and the blood volume in active circulation greatly reduced, due to loss of normal tone in the capillaries and increased permeability of their endothelial walls, permitting leakage of plasma out into the tissues. 50% of the plasma might be lost in a few mins., giving oligaemia, and concentration of the blood, the red cells and Hb. being markedly raised, even 50 % above the initial values. Imbibition in all the cells



of the body was increased at the same time. As the blood was not returning in sufficient amount to the heart to fill it in diastole, the circulation failed. In this condition, Hooker(495) and also Rich(551) showed by direct microscopical examination that a large number of the capillaries opened up.

Healthy unanaesthetised cats, Dale(477) found, could deal with considerable amounts, up to 10 mgrms. per kilo. Haemorrhage and anaesthesia with ether and  $\text{CHCl}_3$ , and removal of the adrenals after one day, enormously lowered the resistance, as in Delayed Wound Shock. The action of the anaesthetic persisted after most of it was eliminated e.g. after  $\frac{1}{2}$  hr., and was probably due to some lasting depression on the mechanism of resistance to Histamine. Nitrous Oxide, however, had very little such effect.

Gum-saline, Bayliss(330) found, might restore the blood pressure completely. By thus raising the B.P. and restoring the blood volume, it probably allowed elimination of the toxic substance.

#### (b). OCCCLUSION OF BLOOD VESSELS.

By this method the circulation is cut off from a large part of the body for some time. Temporary clamping of the Inferior Vena Cava, Thoracic or Abdominal Aorta produced typical signs of shock.

Janeway and Jackson(191) in 1915 clamped the Inferior Vena Cava for 2 hrs. and obtained typical signs of shock. Bayliss(327) and Erlanger(456) confirmed these results. Similarly, 2-hr. partial occlusion of the Thoracic Aorta and of the Abdominal Aorta(191, 456). Mann(347)

tied off all the structures of the four limbs, except the main artery, with iron wire ligature.

These methods entail the operation of various factors, Reduction of the total blood volume in active circulation presumably occurs to a considerable extent and probably plays the main part. Associated with this are marked reduction in the volume flow of blood to, and local anaemia of, the parts supplied. (See CIRCULATION).

(c). FORCED VENTILATION OF THE LUNGS.

Yandell Henderson(91) introduced this method. Unless the pumping used is very vigorous, this method may fail. It is recognised that the artificial ventilation used in these experiments is much greater than the animals could produce themselves. (See RESPIRATION).

(d). INTRAVENOUS INJECTION OF ADRENIN.

This method was used by Bainbridge and Trevan(228), and by Erlanger and his associates(457). Relatively large quantities of adrenin were injected for about  $\frac{1}{2}$  hour. Bainbridge and Trevan(228) injected 6-11 ccst of 1:1000, a small quantity every  $\frac{1}{2}$  min. for 20 mins.

Erlanger and his coworkers(457) and Crile(565) also obtained similar results. Y. Henderson(254), however, injected smaller doses and failed to obtain signs of shock. He used 0.5 - 1 cc. a min. of 1:10,000 for 2 hrs.

The causal factor in this condition was supposed by Erlanger(457) to be the obstruction of the blood-flow through the liver. But plugging the portal radicles in the liver with lycepodium spores did not produce a shock-like condition like adrenin injection. Therefore, increased resistance in the portal-hepatic circulation, giving accumulation of blood in the portal

area was not the cause. (See ADRENALS).

(e). EXCESSIVE HEAT AND COLD.

These agents applied in various <sup>ways</sup> produce shock. Mann (347) applied them to the blood for 2 to 3 hrs. He found that, with excessive cold applied by immersion in ice-cold water, or by introducing ice into the abdominal cavity, the rate of the heart-beat was greatly decreased, and the amplitude of the beats increased.

(f). INTRAVENOUS INJECTION OF STRYCHNIN.

In often-repeated doses, strychnin may eventually produce a fall of arterial pressure, according to Crile (559). Leonard Hill (63) supposed that, while strychnin at first converted depressor into pressor reflexes, it later paralysed the synapses of the pressor fibres with the vasoconstrictor centre.

(g). OVERANAESTHESIA.

Mann (376) found that, experimentally in dogs, high tensions of ether could readily produce signs of shock. By varying the tensions, he could parallel the various stages. In many instances, he believed that this had been confused with shock and so the data had been contradictory. (See CAUSAL FACTORS—ANAESTHESIA).

All these methods of shock-production in animals may be grouped, as Gesell (450) suggested, as initiating factors. These ultimately lead to changes in the tissues, e.g. cell damage, increased permeability of the cells, transudation, decreased blood volume, slowing of the blood stream, etc. These represent the sustaining factors.

SECTION VIII. CENTRAL NERVOUS SYSTEM.

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The changes in the Central Nervous System are obviously of great importance, whether they be primary or secondary, as the Central Nervous System largely controls and regulates the activities of the rest of the body. Hence the brain may be regarded with Matthews (556) as the "master tissue of the body". This regulation takes place, both directly by nerve impulses and indirectly through the blood. In addition to the nervous influence on the various organs and tissues, there is the chemical excitation by various substances, e.g. toxins, lack of oxygen, diminution of  $\text{CO}_2$ , adrenin, etc., and both mechanisms are probably always at work in cooperation or in antagonism, according to the needs of the body.

In the case of Traumatic Shock, the view taken in this Thesis is that both processes again play an essential part in the causation. In Immediate Shock, the nervous stimulation predominates, and the Central Nervous System is profoundly affected, being first excited, then depressed; while in Delayed Shock nervous stimuli initiate the processes that occur in the condition, and the chemical substances continue them.

The chemistry of the brain is peculiar, and suggests that its nutrition would be easily upset by excessive nervous stimuli or deleterious chemical stimuli in the blood. The nerve cells contain no reserve carbohydrate, e.g. glycogen, and no neutral fat (557). Yet their metabolism is very active, both respiratory or oxidative and



nutritive metabolism. It is therefore essential that it obtain abundant oxygen and nutritive material, e.g. glucose, from the blood (558).

It is well known, too, that the emotive condition has a marked predisposing influence on the development and severity of shock, just as it has, though still more, in Commotional Shock and War Neuroses, according to Mott (426). (See CAUSAL FACTORS).

#### WHAT ARE THE CHANGES?

Stimulation of the nervous system, as Delley (387) pointed out, must result in either excitation or depression, and it is probable that the nerve cells go through the processes of activity, fatigue, and finally exhaustion. Of great importance to life are the changes in the vital centres in the medulla, which regulate the mechanisms of the circulation and respiration. These reflex mechanisms are considered under the headings of the circulation and respiration. But all the other reflexes are changed in Traumatic Shock.

In severe Immediate Shock, the nervous functions are more or less fatigued, inhibited, or paralysed. In the more gradual Delayed Shock, the functions are first excited, then depressed, indicating excitation, followed by depression, of the nerve centres. The intellect at first alert becomes clouded; muscle tone becomes lowered, common sensibility is diminished, and the reflexes are diminished or abolished.

Objective changes, such as changes in temperature of

the brain were also studied by Crile, and, post-mortem, microscopical structural changes throughout the Central Nervous System, both in the cells and in the blood-vessels, and changes in electrical conductivity were described by Crile.

The cause of these changes is still "sub judice". It has not yet been proved that afferent impulses cause them, and that they are, therefore, primary and essential signs of Traumatic Shock, as Crile supposed. On the other hand, it has been proved that cerebral anaemia can cause them, and it is probable that the partial and gradual cerebral anoxaemia resulting from circulatory failure in Traumatic Shock is responsible for their production.

#### (1). CLINICAL AND EXPERIMENTAL OBSERVATIONS.

On enquiring regarding subjective symptoms in Wound Shock, Cannon(387) found that the wounds were generally not painful in themselves, especially the large bruising wounds.

#### INTELLECTUAL FUNCTIONS.

In Immediate Shock, the intellect might be more or less paralysed, and the patient semi-conscious. In Delayed Wound Shock, it was not primarily affected apparently. The intelligence often remained clear, and restlessness was more common than somnolence, according to Cowell(224, 340). In severe degrees, however, the patient was generally drowsy, difficult to rouse, and apathetic, but not unconscious. In gas gangrene infection, the brain might be clear to the end.

The memory was unimpaired.

### EMOTIONAL FUNCTIONS.

These might be depressed from the outset, or first exalted and then depressed, according to the type of shock. Exaltation might be signalised by a soldier "carrying-on" in the heat of battle, or by restlessness and shouting; depression by moaning, and by fear.

### MOTOR FUNCTIONS.

In Immediate Shock, the motor power is practically lost in severe degrees. In Delayed Shock, these functions appear to be less affected than the sensory. In the early stages and in slight degrees, the muscular power was not diminished, as tested with the dynamometer, according to Cowell (224, 340). Later in shock, however, muscular prostration develops and may become extreme and generalised.

The involuntary muscles are also inhibited, probably from stimulation of the sympathetic system. In obstetrical shock, Tweedy (578, 583) observed that the muscle of the uterus was much elongated, "retraction reversed". In tubal rupture the tubes were dilated. Inflation and indrawing of the cheeks in respiration, dilatation of the pupils, relaxation of the anus, dilatation of the intestines and bladder, he suggested, were due to relaxation of voluntary and involuntary muscle. Similarly, the abdominal veins might appear empty and yet be relaxed, the contents being about the same but their calibre increased. The arteries were also probably in a condition of "retraction reversed".

### SENSORY FUNCTIONS.

At first there may be an initial hypersensitiveness.

Then these functions, including touch, temperature, and pain, progressively become depressed.

### REFLEXES.

In established shock, the reflexes are profoundly depressed. In Experimental Shock, this depression or loss of reflexes was universally recognised as one of the cardinal signs of shock. The animal in deep shock lay unresponsive to external stimulation. E.L. Porter (375) appeared to show that the reflexes were relatively augmented in Experimental Shock, but his results, while accurate and confirmed by other observers, were found to be capable of a different interpretation.

The organic reflexes of respiration and circulation are also profoundly affected, and are described under these headings.

SIGNS OF GENERAL STIMULATION OF THE SYMPATHETIC DIVISION OF THE AUTONOMIC NERVOUS SYSTEM are also present, both in Clinical and Experimental Traumatic Shock. The evidence in general indicates first excitation, then depression. The signs indicating excitation are as follow: dilatation of the pupils, increased sweating, acceleration of the heart, increased arterial tonus, cessation of movements of the alimentary canal and of digestive secretions, relaxation of bladder wall, etc. Some of these signs were accounted for in a different way, e.g. the perspiration, Crile (75) suggested in 1909, might be due to opening of the duct mouths from contraction of the smooth muscle of the skin and diminished blood supply. As this system is to some extent independent of the



Central Nervous System, it is possible that the cause of the excitation may be different from that of the C.N.S. The internal secretion of the adrenal glands was supposed to be the causal agent by Cannon, Elliot, and others (see ADRENALS). Adrenin increase gave excitation; later, decrease of adrenin and anoxaemia probably cause the depression.

## (2). TEMPERATURE CHANGES.

Mosso (quoted by Howell (620)) showed in 1894 that increased mental activity was accompanied by rise of temperature.

Crile (603) studied these changes in Traumatic Shock. His method was to observe the variations by means of galvanometers with special thermocouples devised to give the temperature within 0.01 deg. C. The constant junction of the thermocouple was immersed in oil at 39 deg. C., the active junction was inserted through a small trephine hole in the skull for the brain, or through an opening below the ribs for the liver. His results (655, 661) showed that in Experimental Shock the temperature of the brain and liver progressively decreased. At first, the brain temperature might show a temporary rise on application of an intense stimulus. Crile pointed out that these signs paralleled the changes in brain-cell structure and in electrical conductivity.

## (3). MICROSCOPICAL CHANGES IN INTERNAL STRUCTURE OF THE NERVE CELLS AND BLOOD VESSELS.

In Traumatic Shock, various histological changes have

been described as occurring in the cells of the Central Nervous System. According to several observers, however, these changes were well within the range of normal variation, and, accordingly, they could not be accepted as a reliable criterion. The general view is, nevertheless, that they do form an index of the state of the cells. Howell(620) pointed out that our knowledge of the nature of the chemical changes that occur in the nerve cells during activity was very meagre. Probably carbon dioxide and lactic acid were formed and oxygen consumed, as in muscle. And the energy of the Central Nervous System came from the chemical changes in the material in the cells, essentially splitting and oxidation of the substances in the cytoplasm. The Nissl bodies, then, though artefacts, might be taken as an index of the amount of stored energy, according to Halliburton(18), and Matthews(556,557,558). Afferent stimuli excited catalytic action and transformed it into kinetic energy, which was transmitted along the nerves to the periphery. Excessive stimulation might lead to exhaustion of the reserve store.

Crile(553,565,655), and Dolley(70,73,74,97) found these changes in Experimental Traumatic Shock in animals, and in fatal Traumatic Shock in man. Mott(231,233,409), and Mott and Uno(581) also observed them to be present in cases of fatal Wound Shock, shock from burns, and "shell-shock", in man, and in "histamine shock" in animals. Turek(501), however, found no brain-cell changes in Experimental Shock, produced by crushing tissues, immediately before or after death from shock.

NERVE CELLS. These showed general chromatolysis, alteration in the nucleus-plasma relation, rupture of the nucleus and cell membranes, disintegration and alteration in staining reaction of the cytoplasm. The Purkinje cells showed an acidophil staining reaction. These changes were described by Dolley(70,73,74,97), as occurring in a definite sequence of hyperchromatism, chromatolysis, and disintegration.

VASCULAR CHANGES. were also noted by Mott(223,409,428,432,581). Dilatation of perivascular and perineuronal spaces, filled with Cerebro-spinal Fluid, with collapsed empty vessels in them, were present, resembling the changes in experimental cerebral anaemia. Small haemorrhages occurred under the pia mater and into the periaventitial sheath, and engorgement of the veins was also present.

Mott also noted that, to the naked eye, the brain appeared in a wetter condition than usual, being soft and oedematous, as in experimental cerebral anaemia. In cases of compound comminuted fractures, fat emboli were present in the medulla and cortex.

#### DISTRIBUTION OF THE CHANGES.

These changes, according to Crile(511), were more or less generalised throughout the cells of the Central Nervous System. They were more marked in the cortex and cerebellum, than in the medulla and cord, and more in the medulla than in the cord.

Mott(loc.cit.) noticed that the smaller pyramidal cells of the cortex were more affected than the larger py-

pyramidal cells, and that the dorsal and ventral nuclei of the Xth. Cranial Nerve were more affected than the nucleus of the XIIth.

Rendle Short(424,425,480)observed that only the sensory cells of the cortex,the Purkinje cells of the cerebellum and Deiter's nucleus,and the sensory basal ganglia,optic thalamus,gracile and cuneate nuclei,were affected.There was no change in the motor areas,i.e.the precentral cortex,the motor nuclei of the pons and medulla,and lenticular nucleus,nor in the spinal cord,posterior root ganglia,and the sympathetic ganglia.

#### (4).CHANGES IN ELECTRICAL CONDUCTIVITY.

Using a special apparatus,Crile(562,591,593,661,655) tested and measured the electrical conductivities of various tissues removed immediately after death.His results showed that in normal animals the conductivity of the cerebrum was higher than that of the cerebellum in adults,but vice versa in the foetus or very young rabbits,and in unconscious man.

In Experimental Traumatic Shock in etherised dogs, and in Operative Shock in man,however,the conductivity of the brain was diminished,that of the liver increased. In the initial stimulation leading to exhaustion,the conductivity of cerebrum and cerebellum showed a slight rise,followed by a gradual and continuous fall;that of the liver,a slight fall,followed by a rapid continuous rise,during the stage of exhaustion.

#### (5).CHANGES IN THE CIRCULATION IN THE BRAIN.

No direct observations have been made as to the effect



cerebral circulation in Traumatic Shock.

Howard(641)stated that some observers found constriction of the blood vessels and anaemia,others dilatation and congestion.He suggested that these differences depended on whether the skull, abdomen,or thorax was opened first.

Robbins(490)studied plethysmographic changes in a trephined stammerer,and found that pronounced emotion always brought about increase of brain volume,accompanied by increased size of pulse.

Suppositions,however,have been made.It may be supposed that the low general arterial pressure in shock finally results in decreasing the pressure on the surrounding cerebro-spinal fluid,and consequently the pressure in the cerebral veins,i.e.the intracranial pressure is decreased.The blood-flow through the brain is also diminished.For,according to the usual view,of the regulation of the blood supply(see Howell(626)), the blood flow is indirectly controlled by the vasomotor effects on the rest of the body.If,therefore, there is reduced volume of blood-flow in the general circulation and fall of arterial pressure,owing to diminished blood volume and in spite of the compensating vasoconstriction,the amount of blood in the brain is lessened,and less blood is driven to it.Local vasomotor nerves,if they exist,may direct the reduced flow through one or other area.

(See also BLOOD and CIRCULATION).

## (6). MUSCLE CHANGES.

Muscle was found by Crile and Dolley(565) to be 50 times more resistant than the brain to low B.P. and consequent anaemia. Contractility of muscle, Crile(565) found, was present in Experimental Shock, contractility both to direct and nerve stimulation.

Microscopically, the muscles showed no change in Experimental Shock, according to Crile(loc.cit.).

Chemical analysis of muscles showed the glycogen content slightly diminished in Experimental Traumatic Shock, according to Crile(555).

## WHAT IS THE CAUSE OF THESE CHANGES?

The changes appear to be the result, and not the cause, of shock. The general view is that these changes are secondary to the anoxaemia due to the circulatory failure, possibly partly to toxæmia due to the absorption of toxins from the injured tissues. Crile(555) in particular, however, assumed that the brain-cell changes were the essential lesion of shock, along with the similar changes in the cells of the liver and adrenals. They were due to noci-stimuli, and caused the other phenomena of shock.

These changes of the Central Nervous System occur in various CONDITIONS, besides Traumatic Shock.

Changes in the Nissl granules were observed by Hodge (quoted by Crile(12) and Howell(620)) in 1892 in the spinal ganglia of birds, <sup>examined</sup> after excessive activity, and in the spinal ganglia of dogs and cats examined after

prolonged electrical stimulation. According to Halliburton(18) the anaesthetics of ether and chloroform were shown by Hamilton Wright to produce a loss of affinity for baso-phil staining in the nerve cells, but this effect passed off. Later, Dolley(70, 73, 74, 97) and Crile(154, 160, 509, 512, 553, 565) described similar changes in the cells of the whole Central Nervous System in dogs, rabbits, etc. as occurring after various conditions of exhaustion, viz. insomnia(553), excessive exertion(554), excessive emotion(615), experimental anaemia and haemorrhage(657), asphyxia, starvation, drug, toxic, foreign proteid, and anaphylactic shock, excessive doses of strychnin, total adrenalectomy, injection of excessive amounts of adrenin, and ether anaesthesia. In all these conditions, Crile asserted, exhaustion was the common underlying factor, and accordingly he supposed that it was the cause of the changes. By exhaustion he meant particularly fatigue of the nerve centres.

Mott found similar changes in Commotional Shock in man(432), and in Histamine Shock in animals(531).

The temperature changes, also, Crile stated, occurred in exhaustion from any cause, as well as in Traumatic Shock, e.g. from excessive exertion. Increase of temperature occurred in the excitement of ether and nitrous oxide anaesthesia(615).

Similarly, the electrical changes were found by Crile in other conditions besides Traumatic Shock, e.g. insomnia(553) emotion(615), infection, toxic, foreign proteid, and anaphylactic shock(510), thyroid feeding in large

doses (the changes being reversed by adrenin), iodoform (519), acid injection (alkali giving the opposite changes), adrenalin, strychnin (604), but not by anaesthesia alone, e.g. ether, urethane, nitrous oxide, and morphin.

Diminution of glycogen content of muscles also occurred after excessive exertion, according to Crile (554).

### CAUSAL FACTORS.

The changes in the Central Nervous System may be primary to the changes in other systems, or secondary. From a consideration of the evidence, it would seem that they are probably secondary. In the production of these changes from trauma, there are various possible processes that may take place (see CAUSAL FACTORS - TRAUMA). Some stimulation of afferent nerves inevitably occurs. These may be the pressor or depressor nerves of the circulation, the inhibitory or accelerator nerves of the heart, or the inhibitory or augmentor nerves of the respiration. The resulting reflex effects may initiate the train of following events, or a relatively primary fatigue of the nerve-cells, supposed to result from too intense or too long afferent nerve stimulation, or an increased resistance at the synapses, due to prolonged stimulation, may offer an explanation.

On the other hand, trauma may cause a toxæmia due to the absorption of toxins set free in the injured tissues. Circulatory failure may thus be brought about, and the consequent cerebral anoxæmia may be responsible.



# 1. STIMULATION OF AFFERENT NERVES.

Suppositions were drawn from OBSERVATIONS OF THE CLINICAL SIGNS. In the case of Immediate Shock, the sudden onset could readily be explained on the hypothesis of a nervous influence. Crile(159) observed that emotion, especially fear, had a powerful effect on the organism. It is common knowledge that phlegmatic patients withstand operation much better than nervous "high-strung" ones.

Suppositions were also drawn from OBSERVATIONS ON THE EFFECTS OF TRAUMA on the tissues, in support of this possibility. These observations, however, are capable of other explanations. (See CAUSAL FACTORS - TRAUMA).

PARTICULAR INSTANCES of the action of trauma introduce a number of other factors, besides stimulation of afferent nerves, and therefore deductions from them are of little value in this connection. The action of trauma on the limbs appears to be the most uncomplicated case, though here, especially if muscle destruction be present, toxæmia may be the main factor. Burns and scalds are complicated by the presence of diminution in the excretory power of the skin, which, if extensive, might result, according to Howard(641) in congestion of the internal organs. Irritation of sensory nerves, however, followed by toxæmia, are probably also both responsible for the effects. Exposure and manipulation of the abdominal viscera, e.g. in operations, involves several factors, viz. reflex changes in the circulation from intermittent tension on the nerves and blood-vessels of the

mesenteries; splanchnic congestion with consequent loss of blood volume in circulation (see Mann (253)), from the handling; increased heat loss and possible loss of carbon dioxide by ventilation from exposure of the peritoneal cavity; toxic absorption from the walls of the gut. Severe blows on the thorax and abdomen, without serious internal lesion, give reflex nervous changes of circulation and respiration, due probably to excitation of the sympathetic plexuses, e.g. the solar plexus, acting on the medullary centres. In acute abdominal conditions, e.g. perforated gastric ulcer, acute haemorrhagic pancreatitis, etc. the "shock" may be due to this agent from the sudden severe irritation of the peritoneum, or to splanchnic nerve stimulation from the affected organ, as well as to toxæmia.

#### DIRECT STIMULATION OF AFFERENT NERVES.

It was at first generally supposed that such stimulation might produce Traumatic Shock. Many observers, however, began to notice that this method was not generally effective in producing Experimental Shock. They therefore resorted to exposure of abdominal viscera and other more effective methods.

Porter (45, 46, 47), who was one of the first to doubt the generally accepted view, experimented on animals, and found that prolonged stimulation, either electrical or mechanical, of the great nerve trunks always failed to produce signs of shock, provided hæmorrhage, opening of the abdomen, reflex cardiac inhibition, etc. which brought in circulatory factors, were not present. Marked

fluctuations of blood pressure level, pulse and respiration rates occurred, especially under light anaesthesia, but quickly subsided on cessation of the stimulation. This temporary effect was therefore not shock.

In such experiments, the longer the animal was kept on the table, the lower fell the blood pressure, probably from the general exposure, as Leonard Hill (63) pointed out, as well as from the prolonged anaesthesia, loss of blood volume from exposure of large surfaces, and splanchnic vasodilatation, congestion, and transudation from obstruction of venous return.

Porter's results were confirmed by other observers, viz. Webster (129), L. Hill (63), Mann (142, 347), Janeway and Ewing (148), Guthrie (255), and Erlanger (257). Janeway and Ewing (148) concluded that trauma to sensory nerves in an unconscious animal was a wholly subsidiary factor. Guthrie (255), however, found that brachial nerve stimulation in dogs, though it often failed to produce a marked fall of blood pressure, occasionally produced shock. Mann (253) found that nerve stimulation in etherised animals never produced shock.

On the other hand, several observers reached contrary conclusions, viz. that persistent afferent nerve stimulation could produce shock. Wiggers (372) found that stimulation of the central end of the cut sciatic might produce "central nervous system shock" and death, or recovery might set in after 2-5 hrs. Circulatory changes were always present, though fall of blood pressure might be absent, the blood pressure being maintained

by other factors.

After elimination of this factor, contrary conclusions were again reached by different observers. By cutting the spinal cord, or by injecting a local anaesthetic, Crile(12,561) and Mummery(30) found that trauma applied to the cut-off area did not produce signs of shock, such as fall of arterial pressure, nor brain-cell changes nor changes in electrical conductivity(519). Other observers, however, found that trauma still had the same effects after the injured part was denervated by cutting the nerves(see BLOOD and CIRCULATION—TOXAEMIA).

#### HOW DOES AFFERENT NERVE STIMULATION ACT?

This stimulation may act in various ways, viz.: (1) by the production of reflexes, (a) circulatory, (b) respiratory, (c) generalised inhibitory; (2). by causing (a) an increased synaptic resistance, or (b) fatigue of the nerve cells.

##### (1). Reflexes.

(a). Circulatory. The general view appears to be that afferent nerve stimulation, when of any significance, exerts an influence by producing a reflex fall of blood pressure, or a reflex inhibitory effect on the heart. L. Mummery(20) found that moderate manipulation of the abdominal viscera produced shock more easily than gross injuries, especially if the parietal peritoneum, peritoneal ligaments or mesenteries were pulled on. Mann(253) found that mere exposure of the viscera gave little or no fall of blood pressure, but pulling on the



viscera gave a slight fall. Clinical observations in cases of Operative Shock led Malcolm(579,582) to conclude that nerve irritation caused reflex circulatory changes. He supposed that intense contraction of the arterioles was present, as indicated by the initial rise of blood pressure, strong beating of the larger arteries while the radial pulsation was lost and the tissues became pale. Presumably some irritation of sensory nerves was present due to the operative trauma, and probably caused these reflex changes. According to Mann(347,376), however, nerve stimulation caused death in animals under ether, only by stimulating the nerves that inhibit the respiration or heart, e.g. the superior laryngeal. In fine, reflex circulatory effects, in comparison with the numerous other causal factors, play a very subsidiary part.

(b). Respiratory. Yandell Henderson(360) supposed this factor to be causal. The stimulation of afferent nerves produced reflex acceleration and augmentation of the respiration, and consequent diminution of carbon dioxide in the blood and tissues (acapnia). Under light ether, only the pain sensation might be abolished, and the rather hyperpnoea might then cause shock.

This process, however, probably only takes place in exceptional cases. (See RESPIRATION).

(c). Generalised Inhibitory Reflex.

Meltzer(36,55) suggested that in severe injuries the functions of the spinal cord were inhibited, and as a result

eventually those of the medulla, and so shock was produced. In shock, the motor and inhibitory equilibrium was upset, and there was a tendency to inhibition. Observation had shown Meltzer(36,55) that, after the abdomen was opened experimentally, peristalsis was inhibited. Meltzer and Auer observed this on the caecum of the rabbit in particular. Exposure to air and cold was not the cause, for, if these factors were eliminated by leaving the abdomen intact, the movements of the stomach and caecum of the rabbit were inhibited, when the skin of the abdomen was incised, as could be seen through the intact abdominal wall, the hair having been cut. Nor was pain the cause, for, after section of the upper dorsal spinal cord to eliminate it, the change still occurred. An inhibition reflex through the splanchnic nerves must therefore be the cause, and, as after the spinal cord was destroyed and the abdomen opened, the movements stopped after a time, it must be a local peripheral mechanism.

Cannon's X-ray work(43) confirmed these results. He concluded that dynamic ileus might be of spinal origin, being due to inhibitory impulses through the splanchnics. Inhibition might cause it, e.g. in general asthenia, it might be due to a reflex e.g. from the testicle through the splanchnics, or it might be of local origin in the wall of the gut from paralysis of Auerbach's plexus or intestinal muscle, e.g. handling especially had this effect even after the splanchnics were cut.

In Immediate Shock, it is probable that the cause is

a reflex inhibition of the cardio-vascular and muscle-tone centres, similar to the condition in Goltz's "Klop-versucht", caused by a very powerful stimulus, physical or emotional. On this hypothesis, favoured by Meltzer (55), L. Hill (63), Roger (285), Guthrie (255), and Mann (347, 501), the sudden onset and the signs are most readily explained. Cowell (224, 416) suggested that it was analogous to fainting, though he had had no personal experience of pure "nervous" shock. Guthrie (255) also suggested that in acute psychic shock inhibition probably played a leading role, but in Delayed Shock there was little evidence that it was a factor. Roger (285) also suggested that a violent excitation of the nervous system gave a series of inhibitory reflex changes. These changes might indicate cardiac syncope, respiratory syncope, or nervous shock. Mann (347, 376) also showed that stimulation of the inhibitory nerves of the respiration and heart might cause cessation of respiration or the heart and sudden death. Probably this was sometimes the cause of sudden death on the operating table.

(2) Increased Synaptic Resistance. The hypothesis that afferent nerve impulses were present in the central neurones was adopted by a number of observers. No objective evidence of their existence was available, however, and various experiments were cited as indirect support of the supposition. If this supposition were accepted, then fatigue of the nerve centres became a possible result of these impulses. Sherrington (481), however, show-

showed that repeated stimulation of afferent nerves lessened the capacity to transmit<sup>4</sup> impulses. He suggested that "blocking" occurred at the synapses between the afferent peripheral and central neurones, from increase in the natural resistance against repeated stimulation. This was a protective reaction. He also found that after a "block" had occurred from repeated stimulation, stimulation at another point produced the reflex contraction. Fatigue of muscles was therefore a secondary factor. Leonard Hill (63, 84) also suggested that defective transmission occurred at the sensory synapses as a result of injury. Stimulation of any reflex arc left it momentarily depressed, and excessive stimulation brought on fatigue or changed pressor into depressor reflexes. Porter explained the apparent relative augmentation of the pressor reflex response, as the blood pressure fell, on this hypothesis. As the synaptic resistance increased, so the threshold stimulus rose and stronger stimuli were required. The cause of this increased resistance, he thought, was anoxaemia or accumulation of carbon dioxide.

Under ether anaesthesia, again, the passage of afferent impulses is probably "blocked" by increased resistance at the synapses. Forbes and his coworkers (211, 212, 601) showed that the passage of afferent impulses, as tested with a string galvanometer, was "blocked" probably at the first synapse of the afferent path. With deep ether, the reaction in total resistance was very great, sometimes almost abolished. (See CAUSAL FACTORS—ANAESTHESIA).



The loss of sensibility may be due to this increased synaptic resistance, consequent partly on the repeated afferent nerve stimulation, and partly on the cerebral anoxaemia, resulting from the circulatory failure (see Fraser(474,639)).

The loss of muscle-tone is probably not due to this condition, for Sherrington(481) showed that, if a new afferent path were chosen, the motor reflex again took place. It is probably due to cerebral anoxaemia, like the other changes (see later). In the case of "SPINAL SHOCK", in contrast, the cause of the phenomena, including loss of muscle-tone, was, according to Sherrington(481), the rupture of the descending nerve paths, because the effects appeared to take place in an aboral direction only. The cause of normal muscle tone (see Howell(619)) is believed to be the reflex tonic activity of the motor neurones to the voluntary and involuntary muscles. These paths, according to Sherrington(loc.cit.) didn't originate in the brain, as ablation of the hemispheres gave a much slighter depression. They probably originated in the pons or mid-brain, and also in the cord itself. Pike, Guthrie, and Stewart(54,69) concluded that the phenomena of Experimental Cerebral Anaemia, which closely resembled Spinal Shock, were due to the same cause. Stimulation of inhibitory fibres was not the cause, according to Sherrington(loc.cit.), because the reflexes showed the features of fatigue instead. Similarly in Experimental Cerebral Anaemia, according to Pike, Guthrie and Stewart(54). Nor was irritation by the trauma re-

responsible, because the effect was in an aboral direction almost exclusively, and a later transection two segments behind the first failed to give the same depression. Nor did low arterial pressure cause it, for the head showed no signs of "shock". Section of the lower thoracic spinal cord and section of the upper medulla in front of the vasoconstrictor centre gave "shock", but no fall of blood pressure.

#### (2)b. Fatigue of the nerve centres.

It was supposed that stimulation of afferent nerves resulting from trauma set up afferent impulses that at first excited the nerve cells of the Central Nervous System to increased activity. Continued stimulation resulted in fatigue of the cells, and finally exhaustion. Crile(528) supposed that the internal respiration of the cells was interfered with giving intracellular acidosis, which caused the cytolytic changes, and the various changes in the Central Nervous System. The internal respiration was also interfered with later by secondary causes, e.g. anaemia. In particular, as pointed out by Dolley(387), impairment of the vasoconstrictor centre resulted and a further fall of blood pressure established a vicious circle. This centre first gave overactivity, then a stubborn maintenance of control. Guthrie(255) also suggested that Delayed Experimental Shock was largely due to fatigue of the bulbar centres from ether poisoning and sensory nerve stimulation, which might lessen their resistance to anaemia. He produced profound shock while the eye-reflex still persisted, by ligation of

only one carotid artery. The more profound stages, however, were probably due to failure of the circulation. Rendle Short(480) supposed that the site of the fatigued nerve centres for muscle tone lay in the medulla (and perhaps in the cerebellum), for he found that the nuclei for muscle tone in the spinal cord showed a loss of Nissl granules, and supposed that they were inhibited, paralysed, or fatigued by efferent impulses.

Observations of the Clinical Signs may be explained on this theory, but also, and perhaps more satisfactorily, on the theory of anoxaemia. The muscle power, e.g., was not lost in the early stages nor in the slight degrees. The reflexes were not diminished to any important degree except, as Bayliss(306) pointed out, when the blood pressure had remained low long enough to paralyse the centres from want of oxygen (see later). The changes in muscle, above mentioned, viz. the presence of contractility, and the absence of microscopical changes, also point, on the whole, against the theory of nerve centre fatigue, and in favour of the supposition of "blocking" at the synapses and anoxaemia.

There appears to be no proof, as Bayliss(672) pointed out, that nervous influence is essential for the life of the cells. Wounds healed just as readily in a denervated area, and denervated parts were only more liable to injury because of the loss of sensation. Bed-sores might be prevented in nervous cases by proper care.

In conclusion, in the case of Delayed Shock, this question is still unsettled. It has not yet been proved

that this factor alone may produce shock, and, on the whole, though stimulation of afferent nerves in combination with other factors may cause a gradual lowering of the reflex responses, yet in Delayed Shock such stimulation is subsidiary. Probably it is chiefly operative in initiating the processes which are continued by other factors.

## (2). CEREBRAL ANOXAEMIA.

Anoxaemia due to cerebral anaemia from circulatory failure may cause these changes. For it is well known that an abundant supply of oxygen to the brain is necessary(18). As Cannon(567) pointed out, the brain cells were especially sensitive to lack of oxygen, and even 7 to 8 mins. total anaemia might be fatal. No investigations appear to have been carried out on the brain circulation in shock to prove whether this factor is actually present. It was supposed, however, that the low blood pressure of shock might produce a cerebral anaemia and consequent anoxaemia, and the majority of workers on Traumatic Shock hold this view(see Bayliss 332)).

Emotional fainting in man is probably due to a sudden anaemia of the brain. A strong afferent stimulus is supposed to inhibit the activity of the nervous centres, so that relaxation of muscle tone, dilatation of the splanchnic blood vessels, etc. may ensue. Similarly, in the case of wounds without loss of blood, fainting occasionally took place, though shock might not follow. Immediate



Wound Shock closely resembled syncope in suddenness of onset, and Cowell(146,224)suggested that the conditions were analogous.

In the case of Delayed Shock, the generally accepted conception during the Great War was that it was mainly due to "anaemia"(see Cannon(225))with concentration and stasis of blood in the capillaries, produced by toxæmia from toxins set free in the injured tissues and circulating in the blood. These toxins might act directly on the cells of the Central Nervous System through the blood, and stimulate them chemically, excitation being followed by depression if the process went on. Or the action might be indirect through the failure of circulation induced by the toxins, and this is probably the main process. The nerve cells are then paralysed, may not completely recover, and thus show structural changes. The decreased electrical conductivity and fall of temperature in the brain may be due to the reduced metabolism consequent on this anaemia. The increased synaptic resistance may be partly due to it, and practically all the other nervous changes may be explained in this way.

#### EXPERIMENTAL TOTAL ACUTE CEREBRAL ANAEMIA.

Cerebral Anaemia may develop suddenly or gradually, and be total or partial. In the experimental condition, it is sudden and total, in Immediate Shock it may be sudden and partial, whereas in Delayed Shock it is presumably gradual and partial, and the supply of oxygen to the tissues is probably insufficient. The effects

of the two conditions, however, closely resemble one another, but in Traumatic Shock the effects are less marked, though Guthrie(255) could not differentiate them sharply.

Experimental Cerebral Anemia may be easily produced in hutch rabbits, as Leonard Hill(63) demonstrated, by holding them vertically for a few minutes. Unconsciousness and death resulted.

Stewart, Guthrie, Burns, and Pike(37) studied the condition of the brain centres in total acute anaemia, produced by ligation of the Innominate and Left Subclavian proximal to the Vertebral, or of the Internal Carotids and Vertebrales of both sides. All function of the brain and anterior cord was lost, no reflexes being left. The degree of resistance varied in the different tissues, the muscles and glands being the most resistant, the brain least. In the brain itself, the cerebrum and cerebellum were the least resistant, then the cells of the medulla, and lastly those of the spinal cord and sympathetic ganglia(52). The ultimate limit at which resuscitation was possible was 20 minutes(37, 52, 251). Beyond that, the destruction of many cells of the vital centres prevented restoration, according to Gomez and Pike(72), and generally a rapidly fatal effect resulted.

Good oxygenated blood supply was therefore essential to the life of the brain. Leonard Hill showed that the brain used up oxygen rapidly, as methylene blue staining was rapidly oxidised. When a plentiful supply of oxygenated blood was provided, Pike and his coworkers

(37,251) found that cells soon recovered and respiration, pulse, and blood pressure soon became normal. So much so, indeed, that some hours after restoration of the circulation to the brain, Pike and his coworkers (121,251) found that transection of the upper thoracic spinal cord might be done without the fatal result which occurred in the normal animal. If done soon after, or as soon as respiration and blood pressure were normal, it was fatal. Probably the fatal result was due to the low blood pressure damaging the vasoconstrictor centre, for damaged nerve cells were more sensitive to low blood pressure.

The respiratory and circulatory centres lost their power of functioning about the same time. The respiratory and vasoconstrictor centres were similar in their resistance, though the vasoconstrictor centre was more resistant in cats (37,52,251). Guthrie (255) accordingly suggested that the condition of the vasoconstrictor centre might be roughly indicated by the condition of the respiratory centre. Bayliss (320a) also confirmed these results, but suggested (310) that in man the respiratory centre might be more resistant, as different animals varied.

In the case of Traumatic Shock, similarly, Pike (251) suggested that some physical damage to the nervous system existed. The low blood pressure in shock (and the consequent diminished blood-flow to the brain) was not low enough in itself to produce such speedy death as often occurred. Probably the nervous system was

injured by the anaemia.

With decreased percentages of oxygen, Porter(133) found in experiments that the reflexes disappeared abruptly when the oxygen content of arterial blood reached 4-5 % by volume. Accumulation of carbon dioxide was prevented.

The circulatory changes in experimental cerebral anaemia, as described by Stewart, Guthrie, Burns, and Pike(37), were different from those of shock. The blood pressure showed an immediate rise followed by a fall, along with slowing of the heart from vagus inhibition. Later a second rise occurred, after the cardio-inhibitory centre had succumbed to anaemia. Then it fell slowly to a continuous level, at which it was maintained. After de-occlusion, the blood pressure fell more, then rose.

The Respiration at first stopped, then a series of strong gasps of the Cheyne-Stokes type followed, then it stopped again. On restoration of the circulation, it recommenced suddenly with a gasp, then gradually increased.

Spasms and death or recovery ensued.

Histological Changes in the Nerve Cells were also obtained, similar to those found in Traumatic Shock. Dolley(73, 74, 97) obtained them in cerebral anaemia produced by haemorrhage. Gomez and Pike(72, 251) also found a change in staining reaction after experimental cerebral anaemia, for 10-20 minutes, and then restoration for a few minutes. The small pyramidal cells were the most susceptible, then the Purkinje cells, cells of the



medulla oblongata, spinal cord, spinal ganglia, and sympathetic ganglia. The difference in degree of the changes in various parts might be explained(37) by supposing that their resistance to anaemia varied. Mott(409, 561) also obtained these changes by ligaturing the vertebral and carotid arteries of both sides.

With elimination of this factor of anaemia, by over-transfusion, Crile(155, 513) and Delley(73) found that much more trauma was required, but that trauma might still give fatal experimental shock and histological changes in the nerve cells(561), and changes in electrical conductivity(555). Pike and Coombs(251) found that restoration of the lowered blood pressure of "Spinal Shock" by clamping the Thoracic Aorta restored the damaged brain functions. They concluded that, similarly in cases of Traumatic Shock with severe damage to the cells of the Central Nervous System, there was no or only slight return of function, if the blood pressure remained low. But the functions improved, if the blood pressure were raised artificially.

### (3). OTHER POSSIBLE ACCESSORY CAUSAL FACTORS.

#### TOXAEMIA.

The toxins absorbed from the injured tissues in some cases, at least, of Traumatic Shock, as well as acting indirectly through the circulatory failure to which they lead, may act directly on the nerve cells through the blood.

### FAT EMBOLISM.

Obstruction of the blood-supply to the brain from fat emboli was suggested as a causal factor in some cases. But the evidence appears to show that, though in some cases where the fat of the body has been disturbed it may be a causal agent to a small extent possibly, generally speaking it is not extensive enough, as Mott (409,581) found, to have any significance. (See BLOOD AND CIRCULATION).

### CHANGES IN THE ADRENALS.

The signs of sympathetic stimulation might indicate a reflex effect from excitation of afferent nerves, but they appear more likely to be due to increase of adrenin in the circulating blood, as Cannon (196) suggested. As adrenalin intravenously injected excites the structures innervated by the sympathetic system by direct action on the organs, as shown by Langley, Cannon (197) concluded that increase of adrenin, which he found in the adrenal veins after strong emotion, was the causal factor. In the initial stages of Immediate Shock, this factor probably plays an important part. Possibly, too, excitation of the sympathetic system by nervous influences may initiate the changes and the internal secretion automatically augment and prolong them.

### COLLOIDOCCLASIS.

This might take place, to a slight extent, as in Commotional Shock, in which the changes were probably due to a disturbance of static equilibrium of the colloidal structures in the nerve cells particularly by the force

of the explosion. Mott(426, 531) found intense congestion of the brain and numerous petechial haemorrhages alongside the blood-vessels in fatal cases.

#### WHAT ARE THE EFFECTS OF THESE CHANGES?

In Immediate Shock, the nervous changes are depressive almost from the first, but in Delayed Shock, the nervous system may be excited at first, causing corresponding changes in other systems, possibly as a defence against the injury, later it becomes depressed, signs of shock appear, and vicious circles then arise.

The effects of the diminution of the organic reflexes of circulation and respiration are dealt with under these headings.

The effect of the loss of muscle-tone is to aggravate the circulatory failure. As Leonard Hill(63) pointed out, the loss of tone in the muscles removed the support to the veins and capillaries, the blood-flow tended to stagnate in the peripheral circulation, the blood pressure tended to fall and the heart-output to be reduced. Loss of muscle-tone produced experimentally by the injection of curare was found by Pike to be accompanied by a fall of blood pressure, both in the normal and "spinal" animal. Similarly in surgery, high stavaine anaesthesia sometimes gave a marked fall of blood pressure, probably partly from loss of muscle-tone in the lower parts of the body. Fall of temperature results, too, as Cannon(260) pointed out. Diminution of muscle-tone, however, may be unaccompanied by a fall of blood pressure,

e.g. in nervous disease and under anaesthesia, where, however, the process is gradual and the heart and vaso-constrictor centre are stimulated to compensate.

#### SIGNIFICANCE OF THESE CHANGES.

In Immediate Shock, the nervous changes are probably primary and consist of a reflex inhibition of the medullary centres and the centre for muscle-tone, from an intense stimulus, physical or emotional.

In Delayed Shock, several causal factors may be at work. Mott(531) pointed out that all the causal factors might cooperate to form a vicious circle. The nervous factor may be active as in Immediate Shock, but in less degree, or it may be practically absent. The other factors soon completely overshadow it. Absorption of toxins is the first of these causal agents to act, followed later by lack of oxygen, when the circulation fails.

The excitation of the sympathetic system seems to be a defensive effort on the part of the organism.

THE KINETIC THEORY OF SHOCK was advanced by Crile and supposed that shock was due to exhaustion of the "Kinetic System", viz. the brain, thyroid, adrenals, muscles, and liver, from over-stimulation. These organs converted potential into kinetic energy (motion or heat). That the brain was intimately linked with the liver, thyroid, adrenals, and muscles, Crile(566) concluded from his observations and experiments. The microscopical changes in the Central Nervous System, liver, and adrenals in



Traumatic Shock were apparently of an identical nature. The temperature changes and changes in electrical conductivity appeared to run parallel, and corroborate them. The electrical conductivity of the liver was increased, that of the brain decreased(655). The electrical conductivities, however, were measured on practically dead tissues and might not be applicable to the living. The glycogen content of the liver and voluntary muscles was decreased in Traumatic Shock, according to Crile(655), and in excessive exertion(554), adrenin injection, and total adrenalectomy(655) decrease was again noted. The iodine content of the thyroid, Crile(655) found, was increased in Traumatic Shock, and also in excessive exertion(554), and emotion(615). The activity of the pituitary, he(655) found, decreased in Traumatic Shock.

In the case of the liver, in particular, Crile(604) found that removal of the organ caused death in a few hours. In decapitated animals with good circulation and respiration, and after adrenalectomy, excision did not cause death so quickly. After removal of the liver, the brain temperature fell progressively until death occurred, and chromatolytic changes again appeared in the brain cells. In voluntary muscular activity and in direct stimulation of a nerve, the temperature of the brain and liver varied in opposite directions. Injection of adrenalin, strychnin, acid, and alkali, gave little change in the liver temperature, but marked variation in the brain temperature. The liver, Crile(518) concluded, was the

basic organ for acid elimination. It stored and delivered glycogen, and broke down the acid by-products of energy transformation into gases and acid salts.

Exposure of the abdominal viscera contributed to lowering of brain temperature, and also indirectly that of the liver. On introduction of hot water into the stomach, he(566) found that rise of brain temperature preceded that of the liver. Injection of adrenalin, Crile(605) observed, gave increase of temperature in the brain and thyroid, but not in the liver and voluntary muscles. After removal of the liver, injection of adrenalin gave little change in brain temperature.

All these changes, Crile concluded, bore a direct relation to the vitality of the organs, indicating a reduced metabolism and fatigue, and were the primary changes resulting from the processes of exhaustion.

Still further to explain these changes, Crile(536, 559, 636, 640, 661) formulated an ELECTRO)CHEMICAL HYPOTHESIS. Each nerve cell was an electro-chemical mechanism. The nucleus and body were separated by a selective semi-permeable membrane, and round the cell itself was also a semi-permeable membrane. The nucleus was the positive pole and took the acid stain, the cytoplasm was the negative pole and took the basic stain. The contents of the cell consisted of colloidal solutions. The cells had thus the power of oxidation, only as long as there was a difference of potential between the nucleus and cytoplasm, and this difference was maintained only as long as there was oxidation.

The organs and tissues were multiples of cells, and similarly the organism was an electro-chemical mechanism, depending on physical laws. The brain was the positive pole, the liver the negative pole, the nerves were the wires, and the salts in solution were the electrolytic fluid. An oxidative electric wave passed from the brain, where the oxidation was highest, down the nerves to the muscles and glands, and finally reached the liver, where the oxidation was at the lowest rate. Then it travelled back to the brain, thus completing the circuit. Man, then, was an electro-chemical mechanism, constructed on the pattern of the constituent cells, each of which in itself was an electro-chemical mechanism.

Crile explained by means of this theory many of the phenomena in Traumatic Shock and in life in general. Thus was explained the specific antithetical action of adrenalin on the temperature of the brain, liver, thyroid, and muscles; the increase in electrical conductivity of the brain by iodine and thyroid extract (e.g. in hyperthyroidism) and the decrease after thyroidectomy; the interference with digestion by strong emotion, injury, pain, infection, etc., because the splanchnic processes were inhibited while the brain was stimulated. Similarly, the antithetical effects of fear and faith, and the results of chronic fear, anger, etc.. Similarly, sleep was a period, during which the difference in potential of the batteries, which had been decreased during the day, was restored. In surgical operations, if the "state of negativity" and internal respiration were maintained, no shock resulted.

The "state of negativity" was maintained by (1) exclusion of fear by management, by operating in the patient's room, by morphin, by analgesia; (2) exclusion of traumatic stimuli by local or regional anaesthesia, by gentle handling, by protection of wounds from irritation of the air; exclusion of stimulation by stimulating drugs.

The entire process of maintaining the "state of negativity" and internal respiration was included in the method of "anociation", a combination of methods of pre- and post-operative management and surgical technique. Internal respiration was assisted by administration of fluids, warmth, blood-transfusion, rest, sleep, and avoidance of deep inhalation anaesthesia. Finally, many of the phenomena of life were explained, e.g. oxygen, water, and acids were essential, because oxidation and ionisation, were essential for electrical conductivity.

No evidence, however, existed, according to Bayliss (672), that static charges played any part in the electrical phenomena of the body. Nor was there any foundation for the theory of the generation of "neuro-electricity" in the brain.



SECTION IX. THE BLOOD AND CIRCULATION.

The changes in the Blood and Circulation found in Traumatic Shock, like the changes in the Central Nervous System, are of fundamental importance. Some of these changes are probably primary factors, at least in some cases, while others are secondary to other changes.

According to the view here taken, the carrying-off from the injured tissues of various products formed in the processes of disassimilation, is the primary factor in cases of Traumatic Shock associated with severe muscle destruction, and possibly to some extent in other forms. Fat Embolism, too, though, rarely of importance, may possibly occur in sufficient degree in rare cases to be a primary factor, producing effects by interfering with the passage of oxygen. On the other hand, the transportation to the tissues of oxygen absorbed from the air in the lungs is rendered inadequate to the needs of the organism, and results secondarily from the failure of the circulation.

TOXAEMIA, AS A CAUSE  
OF TRAUMATIC SHOCK.

During the Great War, an hypothesis was advanced that Delayed Wound Shock was a toxæmia, caused by absorption of toxic substances formed by the autolysis of the injured tissues. Both British-American and French observers independently reached the same conclusion.

For Traumatic Shock associated with extensive bruising of muscle, this view appears to have been proved. Shock from burns also appears to be due to a similar agent. But in regard to other varieties of Traumatic Shock, it is doubtful whether and to what extent this factor enters. The chain of events following on the absorption of toxins leads to circulatory failure. Dilatation of the capillaries directly results from the toxic action of these products, and is inevitably associated with stagnation of the blood-flow in them. Loss of total blood volume in active circulation is thus produced by this "pooling" of blood in the capillaries. Consequently failure of the circulation takes place, including progressive fall of blood pressure and volume of blood-flow.

FACTS OF CLINICAL AND EXPERIMENTAL OBSERVATION.

The supposition that this factor exerted a causal influence arose from clinical observations, both in general and in particular.

In general, the time interval that elapsed between the injury and the onset of Delayed Shock appeared to

Cuthbert Wallace(401)to allow for the elaboration of toxins. On the other hand, Baruch(400) supposed that inhibitory nerve processes were taking place. It appeared, again, that Delayed Wound Shock often depended more on infection than on extent of injury. Indeed, "Toxic Shock" was recognised as a separate type(see DEFINITION). With infection from streptococcus or Bacillus Parfringens, rapid effects might be produced, as Cannon(614) pointed out. Wounds of hollow abdominal viscera, the contents of which were rich in toxic products like histamine readily produced shock.

Quénu(397) pointed out that everything that favoured absorption favoured shock, e.g. a small orifice in the skin with extensive muscle damage beneath, removal of a tourniquet, etc. Anything that delayed absorption delayed shock, e.g. a tourniquet applied proximally to the wound.

Suppression of the injured region, if not too long delayed, might cause the shock to disappear, e.g. a quick amputation, or the application of a light tourniquet.

In particular, injured muscle seemed a specially common causal factor. Cuthbert Wallace(334, 401) observed that the cutting of large muscle masses in operations produced shock, e.g. amputation of the hip was more shock-producing than amputation of the shoulder, other factors being equal. Large wounds involving large muscle masses, and small multiple muscle wounds seemed to show a special liability to shock, according to Wallace(401) and Quénu(397). In gas gangrene infection of muscle,

however, it became known (see R. Short (425)) that absorption might begin within 12 hours.

Tweedy (578, 583) pointed out that in obstetrical conditions freshly effused unclotted blood was toxic, e.g. in ruptured ectopic gestation, concealed accidental haemorrhage, haematoma of the vulva, etc.

On the other hand, amputations of crushed limbs, excision of muscle infected with gas gangrene, or application of a tourniquet was followed by marked improvement. Other shock-producing factors, besides muscle-bruising, such as haemorrhage and infection, were eliminated by these measures. Moreover, Crile (439) pointed out that men with extensive wounds of the extremities, with tourniquets applied, might yet pass into shock and die; and, similarly in operations in which tourniquets were kept on, shock might still develop.

Similarly to muscle, the effects of extensive burns probably result from intoxication, possibly, according to Cannon (438), by protein derivatives set free from the area of tissue destruction.

On the other hand, in the apparent absence of toxic absorption, shock might develop. In abdominal operations, e.g. Wertheim's operation for cancer of the cervix uteri, it would appear that absorption of toxic products has little if any role, but in such cases the prolonged nature of the anaesthesia and operation introduce other important factors, e.g. exposure, anaesthesia, haemorrhage, etc.

Bazy (530), however, suggested that toxins from latent

infection might be responsible for Operative Shock in some cases. E.g., in the interval operation for appendicitis, death might result in 24 hours, perhaps from anaphylaxis, shock from the operation itself being excluded. In suspected cases, he gave an intradermic test, and, if it were positive, prepared a vaccine.

Experimental Traumatic Shock produced in animals by crushing muscles, thus imitating the clinical condition as far as possible, was proved to result from toxic absorption from the injured tissues.

Turck(354,501), having first applied an elastic ligature proximally, then bruised the thigh muscles, and waited for autolysis to take place. On removal of the ligature, and especially after massage of the limb, signs of shock appeared, prompt and severe. If the ligature remained on, or if amputation were performed, no shock appeared. If intravenous injection of muscle juice or extract, were done, shock resulted.

Bayliss and Cannon(404), Bayliss(295,316), Cannon(614)) performed similar experiments on etherised cats. They found that rupture and severe bruising of the flexor muscles, produced by hammering them against an iron block without breaking the skin resulted in signs of Immediate, then Delayed Shock. The arterial pressure might show at first a sharp fall followed by a rise. Or no immediate effect might occur for 20 minutes, then a gradual fall took place, reaching after about an hour 80-90 mms. Hg., i.e. shock level. The respiration became increased in rate and shallow, then slower. The pulse



rate showed similar changes.

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### WHAT IS THE CAUSE OF THIS TRAUMATIC SHOCK?

These facts obtained by observations in Clinical and Experimental Traumatic Shock, and in experiments suggested as the cause of the condition toxins absorbed from the injured tissue into the blood. This suggested cause must now be tested, and first of all, other possible causal factors may be eliminated.

#### (1). NERVOUS INFLUENCE.

That nerve influence might be a causal factor was suggested by Crile(439) He asserted that traumatising of nerve tissue alone without touching any other tissue could cause death in animals. He showed that nerve "blocking" by local novocaine infiltration, or by spinal anaesthesia, did prevent Operative Shock. Moreover, he suggested that Nitrous Oxide and Oxygen was a specific preventive in shock through a protective action on the nervous system. Leonard Hill(472) suggested that violent nerve stimulation might evolve these substances in the cells. Enquiry by Cannon(438) of men in Wound Shock, however, showed that complaint of pain was rare.

Elimination of this factor, as shown by Bayliss and Cannon((264), Bayliss(405), Cannon(406)), gave no change. If the spinal cord or the nerves of the limb were cut, so as to disconnect the region from the Central Nervous System, the fall of blood pressure still resulted. Nervous reflex stimulation through the afferent nerves could not therefore be the cause.

Nor was it due to depression or exhaustion of the

Central Nervous System with gradual loss of vasoconstrictor tone. For Cattell (quoted by Cannon (614)), using Bartlett's method (see SUPPOSED DILATATION OF ARTERIES later), found that the rate of in-flow of 3 ccs. of normal saline at constant pressure through the femoral artery of the other hind limb always showed a gradual increase in the time of inflow, i.e. a decrease in the rate.

#### (2). FAT EMBOLISM.

This was not the cause, for, according to Cannon (614), the lungs showed no accumulation of fat, nor did the respirations change, except by becoming more rapid and shallow when the blood pressure fell, and then slower.

#### (3). LOSS OF BLOOD AND LYMPH FROM THE CIRCULATION.

This did not cause it. Though the damaged tissues became much swollen with blood and lymph, yet the difference in weight of the intact and injured limbs was only 10% of the estimated blood volume, according to Bayliss and Cannon (loc. cit.). Bayliss (311, 324) found that after slight loss of blood the fall of blood pressure was greatly increased, while intravenous gum-saline might prevent the fall or restore it. He supposed, therefore, that the toxic substance was thus removed or destroyed.

#### (4). ACAPNIA.

This did not cause it. In the experimental condition Cannon (614) observed no hyperpnoea for some time, and later the respiration was not deep enough. Moreover, if the breathing were kept uniform artificially, shock was produced by muscle injury in the same way.

(5). ANAESTHESIA.

This was not the cause of the condition, because, as the shock deepened, the ether was administered more lightly and yet the circulation did not improve, according to Bayliss and Cannon((404), Bayliss(295, 316), Cannon(614)).

(6). TOXIC ABSORPTION.

These possible causes of Experimental Traumatic Shock thus being excluded, there remains to be considered the giving off of toxic material into the circulation and the absorption of it.

Turck(354, 501) found that the transplanting of autolysed tissue or injecting the extract of autolysed muscle into homologous animals gave death from shock. Bayliss and Cannon((404), Bayliss(405), Cannon(406)) found that, if the aorta or inferior <sup>vena</sup>cava or the iliac vessels were clamped or ligated during the traumatization for 33 minutes, no fall in arterial pressure resulted. But, when the ligature was removed, the blood pressure fell to a low level and signs of shock appeared, especially if the muscles were also massaged. If the ligature were kept on and the limb amputated, no shock occurred.

INTRAVENOUS INJECTION OF CRUSHED MUSCLE EXTRACTS.

The bulk of the experiments show that such injection does cause shock.

Vincent and Sheen(21) showed in 1903 that watery extract of muscle might cause vasodilatation and a temporary fall of blood pressure, even after section of the

vagi or paralysis by atropin. Bayliss(322) found that extract of muscle, which had gone into rigor, produced vasodilatation of the intestines and a fall of blood pressure. This occurred whether the lactic acid in the muscle were neutralised or not.

Delbet(396) also found that the extract from the crushed tissues of animals, especially rats, gave toxic effects when injected into other animals of the same species. Polypnoea, loss of reflexes, and coma resulted. He suggested that the strong meat diet of the soldiers in France during the Great War predisposed to shock, as the carnivorous gray rats and toads were more susceptible than the herbivorous guinea-pigs.

#### INJECTIONS OF BLOOD AND SERUM.

Lindsay and Rendle Short(425) found that 10 ccs. of the blood of a man who had just died of Wound Shock, injected into a rabbit, caused no change.

Recently, however, Cornioley and Kotzareff(572) of Geneva found that injection of serum from an animal with traumatic shock into a normal animal of the same species gave signs of shock, and in large doses even death. They immunised animals with serum, and found that severe trauma did not then give shock, and that the serum withdrawn did not then cause shock in another animal.

CROSS-CIRCULATION EXPERIMENTS.

These offer conflicting evidence, but, on the whole, favour the possibility of Traumatic Shock being caused by toxic absorption..

Crile(156,513,561)found that,if the circulation of two dogs were crossed by anastomosing their carotid arteries and jugular veins and only one dog were traumatised,histological brain cell changes were most marked in the traumatised dog.

Later,however,Cornioley and Kotzareff(572)of Geneva found that,in crossed-circulation in rabbits and with the production of traumatic shock by crushing the muscles in one rabbit,the other also developed signs of shock,including fall of blood pressure,fall of temperature,and somnolence.

Recently McIver and Haggart(589,659)from cross-circulation experiments also reached the conclusion that some <sup>substance</sup> toxic was absorbed from the traumatised area.To avoid exsanguination of the normal animal,they selected the hinder part of the cat's body for traumatization,and by anastomosing the aorte and the inferior vena cava just above the bifurcation,the circulation of that area was taken over by the normal cat.The cats were under urethane and the body heat was maintained.The anastomosis was effected by a paraffined glass cannula.On establishing the cross-circulation,the blood pressure generally (in 9 out of 12 cases)fell to the shock level mostly within 30 minutes.Gentle massage of the traumatised legs caused a drop in pressure.With five controls,



no shock appeared, except in one case. In three cases out of twelve, no fall and no shock occurred.

#### ANALOGOUS CONDITIONS.

The process of analogy from a large number of similar instances also suggested a similar conclusion as to the origin of this condition.

#### "Histamine Shock" .

A condition of shock closely resembling Delayed Traumatic Shock, at least that due to muscle injury, could be produced in etherised animals by an intravenous injection of a relatively large dose of histamine. This condition was discovered by Dale and his coworkers (304, 402, 403, 634), and is described in the section on Experimental Traumatic Shock. These workers showed that in this condition a dilatation of the capillaries, smallest venules, and arterioles, with stagnation of the blood in them, was present, accompanied by constriction of the arteries and veins. Consequently, the blood volume in circulation was reduced, the veins and heart chambers were emptied, and the circulation failed from acute oligæmia. "Histamine Shock" was, therefore, supposed to be analogous to Delayed Wound Shock, in which also a prominent feature was the oligæmia.

#### Acute Toxaemias.

A large number of bacterial toxins also had a similar effect on the capillary circulation, e.g. the collapse of Cholera.

Diphtheria, in the toxaemic stage, as pointed out by

Harding(532)resembled Delayed Wound Shock in certain signs.The reduction in cardiac output,the slight oedema or "lymph-bogging",the increased specific gravity of the blood,changes in the adrenals of hyperchromatism and hypochromatism,were present in both conditions.

Acute septicaemia,gas gangrene infection,the later stage of malignant oedema,according to Howard(641), acute peritonitis,acute infective pancreatitis,etc. resemble Traumatic Shock in their effects,and may be explained by supposing that toxins cause them.

Toxaemia from intestinal obstruction appears analogous also.Whipple and his coworkers(268)found that toxemia, produced by isolating loops of intestine or by duodenal obstruction in dogs,caused signs of shock.If those loops were kept aseptic,however,shock was absent,according to Dragstedt and coworkers(266).

That primary cell injury might be the cause of Traumatic Shock was suggested by the work of Whipple and his coworkers(378,379,380,487,488).Rapid depletion of serum proteins was brought about by repeated bleedings and the introduction of warmed red blood corpuscles,suspended in protein-free,modified Locke's solution,and keeping the the volume of blood removed equal to the volume of blood-cell suspension injected.Rapid depletion of total serum protein could rarely be carried below 1 % without causing a fatal reaction.The increase of serum-protein concentration was at first rapid,probably from a reserve in the body cells,especially the liver,then more gradual,but slow and in striking contrast to fibrinogen,

a blood plasma protein(378).With a meat diet,the regeneration was more rapid(379).

These observers(380,488)found that,after even moderate plasma depletion,preceded by liver injury,a fatal shock reaction took place.Possibly the injury of the liver cells,which was effected by chloroform anaesthesia or phosphorus,and which was thus associated with a fall of blood serum protein,was partly responsible.Regeneration was also delayed by it.E.g.Eck fistula dogs were very susceptible to shock by plasma depletion.They concluded that the liver was probably concerned in maintaining the normal level,which it kept very stable both in health and disease(380).

#### Anaphylactic Shock.

This condition also appeared to be analogous to shock due to toxaemia.

Richet and his coworkers(412)discovered this condition. It was caused by a large number of various substances of animal and vegetable origin.They showed that,three weeks after a preliminary injection,a second injection always produced anaphylactic shock.Dilution of 50 ccs. horse plasma with 2 times isotonic sodium chloride, or rendering the blood hypertonic with 75 ccs.of 20 % sodium chloride, $\frac{1}{2}$  an hour before the injection of the horse plasma into dogs,prevented<sup>it</sup>.Probably these strong doses of salt protected the nerve cells by saturating them,and thus rendering them less capable of fixing the poisons on their protoplasm.

Preceding the signs of anaphylaxis(see DIFFERENTIAL

DIAGNOSIS), according to Widal, was a blood "crisis", viz. sudden destruction of erythrocytes, leucopenia, diminution of blood platelets, and great alteration in coagulability of the blood. This condition of the blood was supposed by Widal and his coworkers to be a biophysical process, a sudden disturbance of static equilibrium of the blood colloids, i. e. haemolysis. They (529) accordingly explained anaphylaxis as being due to colloidolysis or destruction of colloids, as, in addition to the blood, the colloids of all the cells of the body, including the Central Nervous System, were probably affected. This shock was not a chemical process, but an upset of physical balance between colloidal structures. Other observers, including Kopaczewski (570), Sicard (571), and Pomaret (580), adopted similar views. Sicard suggested that the physical process was the same in anaphylactic and arsenical shock. The flocculation of the serum gave obstruction in the capillaries and so anoxemia. Sodium Carbonate, he found, was preventive.

Commotional Shock was believed to be caused probably in the same way, the force of the explosion disturbing the static equilibrium of the colloidal structures. (see DIFFERENTIAL DIAGNOSIS).

Moore (413) regarded shock as a disturbance of balance between the colloids of the blood and cells and the crystalloids. With the diminution in blood volume, there was a relative loss in colloid as compared with crystalloid. The crystalloids, having no colloids to anchor them, therefore tend to pass out. Between colloid and

crystalloid, he imagined a slight molecular union or adsorption.

McDonagh(473) claimed that shock, anaphylaxis, and nitritoid crises, etc. were identical, and all due to upset of the normal H-ion concentration(see later).

#### WHAT IS THE TOXIC AGENT?

The active agent presumably is produced by the catabolism of the injured tissues. Besides crushed muscle, many other tissues may cause toxic signs, e.g. crushed liver, extravasated blood, pinched intestine, according to Cannon(614). Lactic acid and protein derivatives form the chief products in this process.

Whatever this agent is, certain properties may be attributed to it. Bayliss(322) found that it was probably soon oxidised, as the effects of injection of muscle extract, which had gone into rigor mortis, soon passed off. Cannon's experiments(614) indicated that it was apparently limited by the injury. If the blood vessels were tied after the trauma and after the blood pressure had fallen, the pressure might rise then to the original level. Nor was the effect permanent, for, if the injury were not great, the blood pressure might spontaneously be restored.

#### LACTIC ACID.

Fletcher and Hopkins had shown that this substance was formed in excised muscles when they were crushed.

Bayliss(327, 322), Cannon(225), and Macleod(540), however, definitely excluded this substance. If the lactic acid in muscle which had gone into rigor mortis were



neutralised, injection of the extract still gave a fall of blood pressure. The alkali reserve, moreover, was not decreased in the first fall in Experimental Traumatic Shock, produced by crushing muscle, but only during the second fall. The anoxaemia due to this low blood pressure might cause the formation of lactic acid in the tissues, as shown by Araki in 1891, and so a consequent decrease of blood alkali. In the case of experimental shock, due to manipulation of the duodenum, Macleod (540) found an increase of lactic acid in the blood only after the blood pressure had fallen permanently to shock level. The amounts of lactic acid in muscle before and after shock were inconstant. Then, injection of lactic was innocuous in shock from muscle injury, and injection of sodium bicarbonate did not prevent the onset of shock. In the case of Caval and Aortic Shock, Bayliss (loc. cit.) attributed the fall of blood pressure as due largely to the in-flow of blood, containing dilator metabolites, produced by the asphyxia, into the blood vessels, which thus became dilated. Probably, however, the products were partly acid, because the respiration was rapid and deep like that due to increased H-ions.

#### HISTAMINE.

Though suggested by some observers, this substance was not claimed as the active agent by Dale (304, 402, 403). He regarded it merely as a convenient agent in producing experimental shock. It was pointed out that histamine might possibly be formed from the amino acid, histidine, in the hydrolysis of the tissue proteins. But there is

no evidence that histamine itself is the cause of this shock produced by muscle injury, though it probably is given off when the tissues are damaged, according to Cannon(614). Dale and his coworkers(634,635) demonstrated that histamine, and even extract of any tissue, added to perfusion fluid and injected intravenously, caused vascular dilatation, in contrast to adrenin and the posterior lobe of pituitary, which caused vasoconstriction. It seemed probable, therefore, that the toxic agent was of an analogous nature to histamine, though not necessarily histamine itself.

#### PROTEIN DERIVATIVES.

Heidenhain had shown in 1891 that injection of peptone gave a low blood pressure and a marked concentration of the blood. This was probably due to increased permeability of the capillaries, as Starling had shown in 1894. Vincent and Sheen(21), moreover, had found in 1903 that watery extracts from several tissues, including muscle, might give these effects.

Peptones or Proteoses, formed by digestion or autolysis of the injured tissues by enzymes were suggested by Turck(354,445,501). He called the extract which was specific to the species, "cytost", and the immunising substance, "anti-cytost"(538). Quénu(414) at first suggested in 1917 that toxalbumins might be the active agent. Later, however, he, as well as Delbet, simply regarded the products of autolysis of injured muscles as responsible. He suggested, too, that probably the liver was less active, as the non-protein nitrogen in the blood and the

ketone bodies in the urine were increased.

Duval and Grigaut(352)suggested that the nitrogen reserve was the toxic agent, and passed out into the circulation as a result of the disintegration from trauma. Vallée and Bazy considered that anaerobes were the agents in the disintegration.

The non-protein nitrogen in the blood. In the case of Wound Shock, French investigators found an increase. In the case of Experimental Shock from proteose injection, Whipple and coworkers(267)obtained a similar result. After proteose injection in dogs, a great rise, even 100 %, occurred in the nitrogen elimination, reaching highest in the second 24 hours, and falling in 4 days. By previous injection, the animals could be immunised. They suggested that injury of the cells had resulted, with consequent destruction of proteins.

Similar results were obtained by these workers(268)in dogs with isolated loops of intestine and duodenal obstruction. The results here they attributed again to injury of tissue protein with consequent great rise in the nitrogen elimination, caused by the proteose intoxication. Dragstedt and his coworkers(266), however, found that, if the bacteria were removed, or tissue necrosis prevented, or if their blood-supply were completely occluded and they were aseptic, life might continue.

Similar results appeared after acute inflammations and suppurations, e.g. peritonitis, septicaemia, etc., according to Whipple and coworkers(382),(383). 40 % increase of non-protein nitrogen in the blood, especially the urea

nitrogen, resulted. In these cases, intoxication due to rapid autodigestion of tissue proteins presumably was responsible.

In the case of Experimental Traumatic Shock, produced by crushing muscle, Aub and Wu(499) detected an increase in the total non-protein nitrogen. As the shock developed, the total non-protein, urea, creatin, and sugar increased, slightly at first, then markedly, especially the creatin and sugar. The increase tended to run parallel with the degree of shock. The rise in creatin was presumably caused by the muscle necrosis. This increased creatin, however, was not the cause of the shock, because in large doses creatin was innocuous. Other substances like histamine were probably also liberated and might be the cause. Reduction of blood-flow and blood pressure without crushing gave no increase.

#### WHAT IS THE SIGNIFICANCE OF THIS TOXAEMIA?

The view taken in this Thesis regards the causes in the two types of Traumatic Shock as different at least in degree. In Commotional Shock the physical process of colloidoelasis seems to preponderate in causing the condition. In Immediate Traumatic Shock, it seems probable that reflex nervous changes from afferent nerve stimulation due to severe trauma, forms the chief causal factor. Probably the toxæmia takes no part in the initiation, as the immediate onset gives no time for such absorption. In Delayed Traumatic Shock, however, this toxæmia exerts

a dominating influence. It initiates the train of events leading to circulatory failure, and all the secondary processes that take place throughout the organism. The toxins are supposed to cause a wide capillary dilatation. Inevitably associated with this change in the calibre of the capillaries is a fall in the velocity of the blood stream in them, i.e. capillary stasis. The volume of blood in the active circulation is at the same time consequently reduced, the volume of blood-flow to the Right heart is lessened, and the arterial blood pressure is consequently <sup>lowered</sup>, i.e. circulatory failure. Anoxaemia next ensues. With deficient blood-flow, the oxygen supply to the tissues is inadequate, and tissue oxidation and respiration are interfered with. From imperfect oxidation other toxic substances are formed, and, being dilator metabolites, dilate the capillaries still further. A vicious circle is thus completed. This vicious circle explains the progressive nature of the effect, and the want of tendency to recover, after the poison has acted for some time. Secondary changes in the various systems result from this anoxaemia, changes affecting the Central Nervous System, blood, respiration, internal secretions, temperature regulation, etc. (see BLOOD AND CIRCULATION, etc.).

Absorption of toxic substances, then, sometimes produces Traumatic Shock, but not always. In the absence of toxæmia, other factors can produce Traumatic Shock.



OXYHAEMOGLOBIN.

Jaboulay(28)advanced the theory in 1904 that the formation of irritating oxyhaemoglobin might cause shock by autointoxication. He found that the oxyhaemoglobin in shock was more stable, and unreducible to reduced haemoglobin by ammonium sulphide. The oxygen was thus not utilised, tissue oxidation and respiration were arrested, as the oxygen was not passing from the blood into the tissues.

No further evidence, however, seems to have been brought forward in support of this theory.

FAT EMBOLISM AS A CAUSE OF TRAUMATIC SHOCK.

Fat Embolism is usually not a causal factor in Traumatic Shock. But in some cases, it may be partly responsible. The two conditions, however, are distinct, and, when occurring alone, differ in several respects.

Fat Embolism was recognised as an important factor in various conditions such as severe fractures, pyaemia, etc. by German observers from 1860 (see Mansell Moullin (2)). Later, the suggestion was made by several observers, including Czerny and Park(3), that it might be a causal factor in the production of shock.

CLINICAL SIGNS.

These signs were "air-hunger" or dyspnoea, pulmonary oedema, even haemoptysis; rales on auscultation; fat

globuli in the urine, blood, and sputum.

FACTS DERIVED FROM OBSERVATIONS IN CLINICAL AND EXPERIMENTAL SHOCK.

Meltzer(36)pointed out that,if fat embolism were present in Traumatic Shock,clinical signs of it should be observed.These signs ,however,are not generally present. There is no respiratory distress,no prominent veins,no signs of pulmonary oedema.

Bissell(208),however,was the first to demonstrate that fat embolism and shock did sometimes accompany one another.He found a remarkable amount of fat in the venous blood stream,up to 65 % ,in cases of fractures.Though death did not result,in some of the cases,shock developed later.Moreover,as Bissell(873)<sup>pointed</sup> out ,post-operative shock was more frequent in fat persons.Fat emboli,he suggested,might enter by the untied central ends of the veins.

During the War,other observers,including<sup>W.T.</sup> Porter (259, 261,355,446),noted that shock was frequent in shell fractures of the femur and in multiple wounds through subcutaneous fat.In the former cases,the opening-up of the bone marrow allowed the absorption of fat.

Sutton(297)also suggested the causal relationship of fat-embolism and shock in some cases,from his findings at autopsies.He found that,after death from shock,fat globules could be squeezed out of the blood in the sliced lung in 10 % of the cases.This was particularly noticeable in fractures,wounds of fatty tissues,and abdominal wounds with laceration of the liver.

microscopically  
Mott(531)found fat-embolism<sup>^</sup> in the brain vessels in three cases of Wound Shock with compound comminuted fracture and much damage to the soft tissues. However, he did not think it sufficient to cause death. Wiggers (231)found that in Traumatic Shock, the pulmonary arterial pressure was reduced, and concluded that no obstruction existed in the pulmonary circulation, and, in particular, no fat embolism.

In general, most observers, including Cannon(567), have found that the fat is not present in <sup>^</sup>sufficient amount to obstruct the blood-flow.

#### EXPERIMENTAL FAT EMBOLISM.

To test this suggested cause, experiments were performed on animals.

Intravenous injection of oil was practised by many of the earlier investigators of this condition. In its relation to shock, however, it was particularly worked at by Bissell(<sup>273</sup>~~188~~). He injected oil into the jugular vein of cats, and obtained signs of shock, e.g. fall of arterial pressure to half or less of the original level.

His results were confirmed by Porter(259, 446), who found that intravenous <sup>injection</sup><sup>^</sup> of neutral olive oil produced shock. He suggested that the result was due to embolism of the vasoconstrictor centre in the medulla, and not to embolism of the lungs. The viscosity of the blood was greatly increased.

Wiggers(336), on the other hand, concluded that fat embolism and Traumatic Shock were distinct conditions, though, after fractures of bones, the former might be

one of the causal factors of the "shock". In experimental fat embolism, he found post-mortem fat droplets in the capillaries of the lungs. This condition also gave failure of the circulation, associated with fall of arterial pressure, but a marked rise of venous pressure. The pressure in the right ventricle and pulmonary artery was rather high, whereas in Traumatic Shock this pressure was low. He suggested, therefore, that it was not advisable, as it was in Traumatic Shock, to drive the blood from the abdominal veins into the heart and infusions were contraindicated.

Simonds(381) confirmed these results in the case of experimental fat embolism. The fall of arterial pressure was gradual, while the venous pressure rose as the arterial pressure fell. Dyspnoea or apnoea might be present, and artificial respiration did not give recovery. In peptone shock, in contrast, the fall in arterial pressure was marked and sudden, and the venous pressure fell. Respiration was not usually changed, and when it was, artificial respiration might give recovery.

Presumably, fat embolism may act in two main situations: (1) in the brain. Fat emboli on reaching the smallest vessels obstruct the blood-flow. Consequently, the oxygen supply to the nerve centres is interfered with, and the centres, especially the vasoconstrictor centre are injured by the anoxaemia. (2) in the lungs, fat emboli may be supposed to obstruct, in a similar way, the pulmonary circulation. The volume-flow of blood in the pulmonary veins to the left heart would thus be lessened, and thus

the volume output from the left ventricle would tend to be reduced.

Fat Embolism may be present without shock.

Fat Embolism was found in numerous conditions, e.g. granular contracted kidney, severe fractures, pyaemia, etc. It was demonstrated by McKibben(452) that visible fat was normally present in the blood in the blood-vessels of animals, and Rendle Short(425) similarly observed this phenomenon in man.

Fat Embolism may be absent, and yet shock may appear.

In the probable absence of fat embolism, Traumatic Shock may be markedly present. In operations such as laparotomies, Wertheim's operation, amputation at the hip, etc., little fat may be disturbed and yet operative shock may be fully established. In the case of perforating wounds of the abdomen, haemorrhage and infection appear to be much more important causal factors than fat embolism. For, if haemorrhage and perforation are absent, shock is absent; if they are present, shock develops. In the case of amputation at the hip, the dangerous stage, as Bayliss(323) suggested, was not when the femur was sawn through.

In Experimental Traumatic Shock, produced by traumatising muscles, fat embolism was presumably absent, as Cannon(225, 341) found post-mortem no fat emboli in the lungs. More, Bayliss(323) noted that it made no difference whether the femur was broken or not.



What is the significance of Fat Embolism?

In the vast majority of cases of Traumatic Shock, this condition as a causative agent is practically absent. It is, therefore, not the essential causal agent.

But in some cases where the fat of the body is disturbed, fat embolism may apparently be produced in sufficient degree partly to bring about the circulatory failure and the signs of shock. This shock-like condition due to fat embolism differs in some ways from Traumatic Shock, as the work of Wiggers (336) and Simonds (381) indicated. Accordingly, it is probably a distinct condition.

In cases where fat embolism <sup>and shock</sup> co-exist, the former would appear to aggravate the condition, and to be partly responsible for many of the changes in the end-result.

FAILURE OF THE CIRCULATION.

Failure of the circulation is one of the most dominant phenomena in established Traumatic Shock. This failure of the circulation consists essentially in the slowing and eventual stoppage of the movement of blood through the entire circuit of the vascular system, i.e. the time taken for a complete circulation is lengthened. And it seems obvious that this movement of the blood is of more importance than the individual factors concerned in maintaining it, such as the volume, velocity and pressure of the blood-flow, as these vary from point to point, and as one fails another may compensate.

As an index to the state of the circulation, various signs must be noted together. Both in Clinical and Experimental Traumatic Shock, the state of the pulse, the measurement of the arterial pressure, and the general condition have to be judged. In general, the blood pressure has seemed a fairly reliable criterion, though the fall of blood pressure does not always correspond to the degree of shock. Determination of the total volume of blood, which may be really a more fundamental condition, forms a useful confirmatory sign. John Fraser (639) emphasised that the three important changes were the lowering of the systolic pressure, the increased concentration of blood, as shown by the haematocrit, and the reduction of blood alkali.

CLINICAL SIGNS.

The clinical signs in general indicate that the circulation of the shocked individual is failing.

Pallor of the skin is at first well marked. In the later stages, the pallor takes on a cyanotic tint. This is particularly noticeable on the extremities and finger nails.

THE PULSE.

During the development of Delayed Shock, the pulse is not increased in rate at first. According to Malcolm (582), it might become fuller and of higher tension. Then it might be slow in rate, and diminish in size and tension until it became imperceptible, while the carotids still beat strongly and the heart-sounds were loud and clear.

With the development of shock, however, the heart rate progressively increased, up to, say, 144 per minute. Cannon (223, 339, 567) found that the rate was not definitely related to the falls in arterial pressure and in alkali reserve.

The expansion becomes smaller until it is imperceptible. This small pulse indicated, according to Cannon (260), that the output of blood from the heart was diminished.

The passage of the pulse-wave is arrested by slighter and slighter pressure, and the beats are best felt by still slighter pressure. These observations indicate the progressive fall of blood pressure.

The pulsation of the carotid arteries is now also

small and weak. (See Pulse tracings in APPENDIX.B.)

Leonard Hill(472)warned that fallacies should be excluded in taking the pulse.The position of the patient, a physical effort or mental agitation,might alter the findings.

#### Experimental

In the case of <sup>A</sup>Traumatic Shock,Cuthrie(255)noted that the pulse generally varied with the blood pressure.As the blood pressure fell,the rate decreased,though no sign of vagal inhibition appeared to be present,and the force became weaker.Raymond(493)also observed that in dogs the rate decreased,as shock developed.The changes in pulse rate were not marked nor constant.

### PROGRESSIVE FALL OF BLOOD PRESSURE.

In Immediate Shock,a rapid fall of arterial pressure sets in at once.In Delayed Traumatic Shock,the progressive fall in arterial pressure is one of the most characteristic signs.John Fraser(474,639)regarded it as the essential underlying factor in the production of shock.

Low arterial pressure,however,it has been repeatedly pointed out by among others Meltzer(55)and Mann(142) is not necessarily always present in shock.It does not always vary with the degree of shock.In severe experimental shock,the level of arterial pressure may be quite high,even 150 mms.of Hg.,and conversly.Hence,by itself,the sign is not satisfactory.Nevertheless,as an index of the degree of shock,it has been found the most

convenient, and, on the whole, if controlled by observation of other signs, is fairly reliable. In practice, according to Fraser(639), the systolic blood pressure is the most important sign, and is the only exact estimation we have of the degree of shock. If 90 millimetres of mercury or less, it indicates a serious degree of shock requiring immediate treatment.

In the case of Delayed Traumatic Shock, the fall of arterial pressure only sets in after some time. At first, it is probably maintained by extra activity of the vasoconstrictor centre, causing greater contraction of the peripheral vessels. Later, the blood pressure begins to fall, probably as the effect of loss of blood volume overbalances that due to vasoconstriction.

#### FACTS DERIVED FROM OBSERVATION IN DELAYED CLINICAL AND EXPERIMENTAL SHOCK.

From clinical observations Malcolm(58)(582) supposed that in Operative Shock the arterial pressure in the large arteries was raised, in the small arteries lowered. The radial pulse, he noted, might become imperceptible, while the carotid pulse still beat forcibly.

In the case of Wound Shock in France, Fraser and Cowell(221) studied the changes of arterial pressure with sphygmomanometers. They found that the arterial pressure might fall immediately on receipt of the injury, giving Immediate Shock, or not until after an interval had elapsed, giving Delayed Shock. This difference in the time of onset appeared closely dependent on the nature



of the wounds. Serious wounds caused a marked and sudden fall in arterial pressure, moderately severe or trivial wounds often did not lower the blood pressure at first, or it might be slightly raised. But after an interval, a progressive fall ensued. Archibald and McLean (272) found the diastolic pressure more important than the systolic. The former might be low, e.g. 30 mms. Hg., while the systolic was 100 mms. Hg. and shock signs present. French observers generally used the Pachon oscillometer. Brechot and Claret (395) found that a difference of 2.5 or more between the maximum and minimum was a favourable sign, below 2.5 unfavourable. Monéry and Lombard (394) put the "critical level" of arterial pressure at 4 for the minimum, and 7 for the maximum.

During operations Lockhart Mummery (30, 31) used the Riva Rocci sphygmomanometer every five minutes if necessary, and the changes of blood pressure have been studied by various other observers. Moots (217) considered the systolic pressure alone of little value, the diastolic pressure alone much more valuable. But the essential sign was the pressure-ratio, i.e. the percentage of the pulse-pressure divided by the diastolic pressure, the normal being 40-60 %. This gave the first danger signal. If low, say 20%, or high, say 80 %, the prognosis was grave. According to Moots and McKesson (503), 20 % decrease of blood pressure, and 20 % increase of pulse rate indicated danger and possibly the onset of shock. McKesson showed that, after  $\frac{1}{2}$  hour of continued low blood pressure, diastolic of 80 mms. Hg. or less, a pulse-pressure of

20, and a rapid pulse of 120 or more, nearly all the patients died of shock sooner or later.

Polak(391,436)held that the pulse-pressure, i.e. the difference between the systolic and diastolic arterial pressure was a better index of the cardiac strength than the systolic pressure. The normal averaged 35 mms. Hg.. He took it at rest, and after moderate exertion. If no change occurred, the cardiac force was good. During operations, under general anaesthesia, he watched this sign particularly—during anaesthesia, at the close, 6 hours and 24 hours after; in shock, every hour, till reaction set in. (464).

Giddings(463), using the "Tyco" sphygmomanometer in operation cases under general anaesthesia, found that the blood pressure might show a gradual fall, sometimes before the pulse showed any change in rate or quality, sometimes simultaneously.

Wells(613) took readings of respiration rate, pulse rate, and blood pressure every 5 minutes during operations, and Clark(650) also made a similar study.

In the APPENDIX B. of this Thesis will be found a series of blood pressure graphs of readings taken during operations.

In the case of Experimental Shock, produced in various ways, two types may again be distinguished, according to the behaviour of the arterial pressure. In Delayed Experimental Shock generally, the mean arterial pressure showed a progressive fall, slight at first, then more rapid and progressive.

Optical manometers were used by Wiggers(365,372). These instruments were devised to register quick changes in pressure, and depended on the use of the segment capsule devised by Frank(see Howell(624)). Wiggers found that, in the initial stage of shock, the arterial pressure curves showed greater amplitude, a larger primary wave, and a quicker decline in the latter portion of systole, while the intra-ventricular pressure curves were not altered in contour. These changes indicated a diminished volume of blood in the large central arteries, probably from reflex reduction of the peripheral resistance. Later, in the progressive stage, there was a progressive decrease in amplitude, along with simple curves, and the intra-ventricular pressure curves also showed diminished amplitude and a less sustained apex. This indicated that the output from the left ventricle was reduced.

The "critical level".

After the arterial pressure had fallen to 50-40 mms. Hg., the animals, it was noticed by observers including Janeway and Ewing(148) and Guthrie(255), showed little tendency to recover.

In the case of Wound Shock, Cannon(223, 567, 616) suggested that approximately 80 mms. Hg. was the "critical level" of the arterial pressure for man. Above 80 mms. of Hg., reduction of alkali was not likely, but below 80, it generally occurred. Possibly when the blood pressure was above 80 and shock was present, vasoconstriction

was still maintaining it against the reduced blood volume. Starling(106) had also found that below 80 a diminished output of energy by the heart muscle occurred.

Fallacies. Before concluding that the fall of blood pressure is due to Traumatic Shock, one must first eliminate the possibility of analogous conditions being partly or wholly responsible. Haemorrhage and infection, in particular, require consideration. On the other hand, certain conditions sometimes associated with shock may give a rise of blood pressure. In certain gunshot wounds Fraser and Cowell(221) found, a rise of blood pressure occurred; e.g. compound fracture of the skull with intact dura mater, perforating wounds of the skull involving the ventricles, wounds of solid viscera such as the liver and kidney. Drummond and Taylor(290) found that a rise of blood pressure occurred at the onset of gas gangrene infection of muscle, but was accompanied by a corresponding rise in pulse rate and deterioration in general condition.

#### FALL IN THE VOLUME OF BLOOD FLOW.

It appeared to Gesell(450) that, as cell nutrition was closely dependent on the flow of blood, the volume of the blood flow was a more important fundamental factor than the pressure of the blood.

METHODS.

Ludwig's stromuhr is perhaps the best known instrument for enabling one to determine the velocity and volume of the blood-flow in animals. Gesell(448,449), however, used an electrical automatic apparatus in estimating the blood-flow through the submaxillary gland of the dog. On stimulation of the Chorda Tympani nerve, he(449) found that the volume of blood-flow increased along with the secretion of saliva and the electrical variation, but the change varied independently of the secretion and was looked on as a vasomotor phenomenon.

FACTS DERIVED FROM OBSERVATIONS IN CLINICAL AND EXPERIMENTAL TRAUMATIC SHOCK.

Direct observation of the changes in the volume of the blood-flow was practised by Gesell(368). Experimental Traumatic Shock was produced in dogs by exposure and manipulation of the abdominal viscera, and the volume of the blood-flow through the submaxillary was measured. Under the lowered blood pressure from the experimental shock, the basal volume of blood-flow was lessened. The initial fall was much more rapid than the fall of B.P., then much slower, and, again when the B.P. had fallen to 50-40 mms. Hg., faster than the fall in B.P. It had no constant inter-relation with the B.P.. It might be reduced 60 %, or even 85 %, with a rise of B.P. or a constant B.P. respectively, then suddenly checked; then, as the B.P. fell, it might remain constant, decrease, or even increase. The initial decrease greatly exceeded that



occurring during the subsequent fall of the blood pressure to zero. Hence the gravity of this change.

On stimulation of the Chorda Tympani in shock, Gesell found the volume of the blood-flow reduced out of all proportion to the reduction in mean blood pressure. This maintenance of the B.P., he suggested was due to increased tonic activity of the vasoconstrictor centre.

By the injection of gum acacia, he (450) found that, in Traumatic Shock, these changes were duplicated in the reverse direction, as in haemorrhage (see CAUSAL FACTORS). The reduction of blood-flow was greater in falls from the normal level than from lower levels (368).

Indirect suggestions, which seemed to confirm Gesell's results, were offered by the work of Rapport (595). The latter noted in experimental shock a gradual increase in heart-rate, probably due to increase of adrenin in the blood, was associated with only a slight fall of blood pressure. The volume-flow and B.P., therefore, appeared to be unrelated.

Changes in the lymph-flow were found by Mann (142) in experimental shock, using a cannula in the thoracic duct. The flow was first increased, then decreased. The colour changed to reddish, and the coagulation-time was decreased like an exudate.

#### The sequence of changes.

A diminished volume of blood-flow in the veins to the right heart presumably forms an important part of the diminished volume-flow. Y. Henderson (384) suggested the presence of this condition, and Wiggers (365, 372) inferred

it from his study of the dynamics of the circulation.

The venous pressure, which in Delayed Shock rose at first later decreased progressively, and optical manometer tracings of the arterial and intra-ventricular pressures also indicated a diminished volume of flow. This fall of volume of blood-flow to the right heart might be calculated, according to a formula given by Aub and Cunningham (498).

At the same time, less volume of blood is available to the heart for pumping, as Cannon (567) pointed out, and diminished output takes place from the left ventricle. From a study of the various blood pressures in Traumatic Shock, Wiggers (365, 372) found that, as the decrease of venous pressure only took place after the initial stage of shock had passed, i.e. in the progressive stage (or in severe Immediate Shock from the beginning), it was only then that it became effective in reducing the output of the left ventricle, and in causing the mean arterial pressure gradually to fall. This result took place in spite of the protecting acceleration of the heart.

Consequent on the gradual reduction in the output of the left ventricle, fall of arterial pressure resulted, when the volume of blood fell below the minimum capacity of the constricted arterial system, as Cannon (567) pointed out.

## WHAT IS THE CAUSE OF THE CIRCULATORY FAILURE?

The main cause of the circulatory failure in Traumatic Shock, according to the view taken in this Thesis, is a loss of blood from active circulation. It might be supposed, however, that changes in any of the chief factors maintaining the pressure and velocity of the blood-flow, viz. change in the heart beat itself, change in the calibre of the vessels, or loss of blood from the active circulation, might cause the failure, being assisted, possibly, by accessory factors such as loss of muscle tone.

### 1. HEART BEAT.

Decrease in rate or force of the heart beat would cause a fall of pressure and velocity of blood-flow throughout the system. Either the heart muscle or the cardiac nerves might be responsible. But this factor will be shown not to be important. It has been found that the cardiac mechanism is not primarily affected in shock, though prolonged lowering of blood pressure will eventually and secondarily impair the functional activity.

#### (a). HEART MUSCLE.

Observations on the state of the heart muscle in Traumatic Shock suggest that it is unimpaired in the initial stages, and only fails secondarily to the anoxaemia of the advanced stages.

It was a common clinical observation that, if the blood volume were increased by intravenous infusion or blood transfusion, the blood pressure returned to the normal level, at least temporarily, due probably to the increased output of the left ventricle. As Mann (142) suggested, the heart presumably recovered and was therefore not responsible.

Malcolm's observations (582) in clinical shock indicated that the heart beat strongly at first, and only weakened later.

In the case of Experimental Shock, it was a common clinical observation that the heart remained beating until the very last, as in Crile's experiments (12) (559). In experimental shock produced by the injection of bacterial toxins, Romberg (quoted by L. Hill (63)) found that compression of the abdomen or of the descending aorta gave a rise of arterial pressure, due probably to the increased volume flow to the right heart and the greater ventricular output. The heart muscle, therefore, could respond well to better filling, and was not exhausted.

In the case of Asphyxia, which he regarded as a common cause of Traumatic Shock, Henderson (96) found that it was associated with an increased tonus of the heart muscle, which condition thus differed from that of the other organs. As the venous pressure, which was required to be increased for the diastole of the heart, was diminished, he looked on this hypertonus as an important contributing factor of the condition.

If the blood pressure were very markedly increased in experimental shock, Mann(142) observed that the heart responded well. He produced constriction of the arterioles by the injection of adrenin, and cut off inhibitory impulses by section of the vagi, and found that the heart muscle was quite able to raise the B.P. to a high level. Similarly, by increasing the intracranial pressure and cutting the vagi.

In the case of Experimental Shock produced by exposure of abdominal viscera, Morrison and Hooker(188) found that the portal, as well as the systemic, venous pressure fell, while the jugular pressure remained practically unchanged. These changes, which were confirmed by Gasser and Erlanger(454), indicated that the heart was able to pump on efficiently all the blood that came to it.

Wiggers(365, 372), from a study of the dynamics of the circulation in Experimental Shock, found that the cardiac discharge was at first gradually increased, along with increase of effective venous pressure, but a fall of mean arterial pressure. Only later was the effective venous pressure and output of the left ventricle reduced.

All these observations, then, indicate that the heart muscle is not primarily changed in shock.

Failure of the heart muscle, however, comes on secondarily to failure of the circulation when the oxygen supply is inadequate (anoxaemia).

Pike, Guthrie, and Stewart(53) in their studies of resuscitation after experimental cerebral anaemia, concluded that the continued normal activity of the



heart was dependent on a proper blood pressure.

Markwalder and Starling(126)also showed that,if the heart was to be properly supplied with blood,it was necessary to maintain the B.P..In the excised heart-lung preparation with a cannula in the coronary sinus, the output from the coronary sinus was dependent on the arterial pressure,which should be 90 millimetres of mercury or over.If the B.P. fell below 80 mms.of Hg., the cardiac contraction began to weaken.

Paterson(172)found that increase of carbon dioxide or hydrogen-ion concentration in the blood caused the heart to fail.He used the isolated heart-lung preparation from dogs or cats under chloroform-ether mixture. On the other hand,adrenalin dilated the coronary vessels and increased the rate and strength of the ventricular contraction,and carbon dioxide and adrenin gave a faster and faster contraction and longer relaxation,so that greater filling and maximum output resulted.

#### (b).CARDIAC NERVES.

The heart beat is also dependent on the nervous mechanism of the heart,as well as on the condition of the heart muscle,and it has been suggested that this mechanism is at fault in producing the circulatory failure.Either paralysis of the inhibitory nerves or excessive stimulation of the accelerator nerves were viewed as possible causes.While both views have been rendered untenable in respect of Delayed Shock,it still remains possible that such factors may be,at least partially,causal in the case of Immediate Shock.

Observation showed that, in Traumatic Shock as the blood pressure fell, the rate of the heart beat became increasingly rapid.

In the case of Experimental Shock, it was found that, after death, the heart, as well as the arteries, appeared contracted and empty, while the veins were full, as in Crile's experiments (12, 75).

(1). INHIBITION OF THE CARDIO-INHIBITORY CENTRE.

Howell (24) suggested in 1903 that this factor might occur in shock. He distinguished two forms of shock, cardiac and vascular. In cardiac shock, the pulse was very rapid, but full, probably from inhibition of tonus of the cardio-inhibitory centre, and the blood pressure was good. In vascular shock, the pulse was again very rapid, but the blood pressure was low, 40 to 20 millimetres of mercury, probably from inhibition of the tonus of the vasoconstrictor centre.

In the case of Immediate Traumatic Shock, the suggestion was made that the cause here was a reflex inhibition of the Central Nervous System, and especially of the medullary centres, such as the cardio-inhibitory, vasoconstrictor, and muscle-tone centres. E.g., Janeway and Ewing (148) suggested that, in the early stages of experimental shock, produced by evisceration and handling of the abdominal viscera, the cause was probably inhibitory afferent nerve impulses. No direct observations, which might indicate the presence of this inhibition, appear to have been made in the case of Immediate Shock.

In respect of Delayed Traumatic Shock, on the other hand, experiments, made to test the condition of the cardio-inhibitory centre, have shown that the centre is not primarily affected, and that its inhibition is not present in Traumatic Shock.

Mann(142) found that, after section of both vagi, experimental traumatic shock did not develop more quickly. The responses of the centre, both to reflex and direct excitation were found by experiments to be unimpaired. It thus appeared that, far from being inhibited, the centre was in tonic activity. Mann(loc. cit.) showed that, in experimental shock if the central end of the cut vagus were stimulated, the heart slowed. If the other vagus were cut, no slowing took place. Similarly, direct stimulation by increased blood pressure, produced by injection of adrenin, or from increased intracranial pressure, gave rise to slow heart beats, which disappeared after section of the vagi. These findings were confirmed by the work of Rich(588).

## (2). OVER-STIMULATION OF THE ACCELERATOR FIBRES.

This possibility was suggested as the cause of the fall of blood pressure by Blum in 1876, and later the same view was adopted by Boise(48,56) in 1907. This excessive reflex stimulation of the accelerator fibres would give acceleration in the heart rate, and according to Boise tonic contraction of the heart and arteries.

The hypothesis appears to rest entirely on supposition. Boise(48,56) observed that, after death from sudden fright, the left ventricle might be found ruptured. He supposed

this result to be due to tonic contraction, consequent on over-excitation of the accelerator nerves. The depressor reflex from stimulation of the testes or the brachial plexus, he supposed to be an indirect effect of the same factor. The gradual decline of blood pressure and slowing of the heart from manipulation of the intestines, Boise suggested, was due to irritation of the inhibitory fibres of the vagus. The treatment, if this were the cause of the fall of B.P., would be to stimulate the cardio-inhibitory centre, and thus antagonise the accelerator effect. Rise of B.P. would then take place, probably, according to Boise, from the lessening of systole and the prolonging of diastole. Boise therefore used *verstrum viride* or *veratrone* in large doses in Experimental Shock.

It is not the cause of shock.

Observations of the state of the heart in shock showed that it was not primarily affected; e.g. restoration of the blood pressure by infusion of blood or gum-saline was associated with a vigorous return of the heart beat.

In the absence of the accelerator mechanism, shock may be present. After removal of the stellate ganglion (and so of the accelerator fibres), Crile (12) found, trauma might not produce a fall of B.P.. Boise interpreted this result as being due to the absence of the causal factor. Seelig and Lyon (98), however, found that in the absence of this factor shock was produced just as readily. They obtained shock after section of both accelerator fibres

and vagi, or after removal of the stellate and coeliac ganglia, which thus cut off the accelerator nerves. Boiss (56), however, explained this result as being due to the escape from cutting of some of the accelerator fibres.

CONCLUSION. It follows from the above evidence that insufficient action of the heart is not the cause of the progressive fall of blood pressure. Neither the heart muscle, nor the two antagonistic sets of cardiac nerve fibres, inhibitory and accelerator, are responsible.

On the contrary, the heart is primarily intact in shock. It even responds by increased effort to counteract the low B.P., both the heart muscle and the balanced nervous mechanism contributing.

Finally, after the circulation fails and anoxaemia sets in, the heart muscle fails secondarily.

## 2. DILATATION OF THE BLOOD VESSELS.

Increase in the width of the vessels would diminish the resistance to the flow, and cause a decrease in arterial pressure.

The small arteries, it was well known, were subject to dilatation and constriction, controlled by the vasomotor nerves, and it was at first supposed that dilatation of these arteries had occurred, due to failure of the vasomotor mechanism. In the case of Immediate Shock it is possible that inhibition of the vasoconstrictor centre giving dilatation of these arteries causes the sudden drop of blood pressure. No observations seem to have been



made in this connection. In respect of Delayed Traumatic Shock, investigation demonstrated that the small arteries were not dilated, but constricted, and that the vasomotor mechanism was not exhausted but over-active in a protective effort to compensate for the fall of blood pressure.

The veins also engaged attention. It was supposed that the veins, especially of the splanchnic circulation were dilated in Traumatic Shock, but this hypothesis also proved to be erroneous.

Attention became directed during the War to the capillaries and it became demonstrated that, in Traumatic Shock dilatation of the capillaries existed. In consequence, the arterial pressure tends to fall and the venous pressure to rise. This tendency, however, is counteracted to some extent by another factor, viz. constriction of the small arteries (and veins), which tends to have the opposite effect. Associated inevitably with this wide-spread capillary dilatation is a marked slowing in the velocity of the blood-stream in the capillaries. At the same time, the capillary blood becomes concentrated, probably losing plasma by transudation through the capillary walls, which have been rendered more easily permeable by the action of toxins on them.

#### (a). SUPPOSED DILATATION OF ARTERIES—VASOMOTOR NERVES.

Through the vasoconstrictor nerves which are in tonic activity, the small arteries in particular may vary in calibre or tone, and thus regulate the general arterial pressure and the distribution of blood to the various

organs. These fibres originate in the vasoconstrictor centre in the medulla, whose tonic activity is maintained from constant reflex stimuli. The tonicity may be either increased by stimulation of pressor fibres, or decreased by stimulation of depressor fibres.

The hypothesis was suggested that failure of the vasomotor mechanism was the cause of shock. It was supposed that dilatation of the small arteries must cause the fall of arterial pressure. In Traumatic Shock, sensory stimuli irritated the pressor nerves so excessively, that the vasoconstrictor centre was over-stimulated, and accordingly became depressed, exhausted, or inhibited. Leonard Hill (63) suggested depression of the sensory synapses. The afferent pressor impulses were thus weakened, or changed into depressor impulses.

Analogous instances of this supposed reflex vasodilatation of the small arteries were well known. Goltz had noticed that light rapid taps on the abdomen of the frog caused standstill of the heart and reflex paralysis of the blood vessels of the abdominal cavity. It was known that, in animals under chloral, stimulation of afferent nerves, which generally gave a rise of blood pressure, produced a fall. And many other examples of reflex vasodilatation were well known.

Again, experimental destruction or paralysis of the vasoconstrictor centre also undoubtedly produced vascular dilatation of the splanchnic or skin areas. Destruction of this centre might be produced by section

of the cervical cord or lower medulla; by pithing (see L. Mummery(30)); by exposure of the medulla to the air; by injection of 2 % cocaine into the medulla. Crile(560) found that, after the application of 2 % cocaine, stimulation of the sciatic nerve, or the injection of strychnin gave no pressor effect, whereas injection of adrenin gave a rise of arterial pressure. Casser and Erlanger(454) found that, after excision of the abdominal sympathetic chain and section of the splanchnic nerves, Experimental Traumatic Shock developed faster. These facts merely indicate, however, that compensation by vasoconstriction in a large part of the body was prevented.

Malcolm(39) emphasised that a very low blood pressure did not necessarily result from a break-down of the vasomotor mechanism, but that it might be largely due to ~~loss~~ loss of blood volume. In cases of haemorrhage, e.g., where no exhaustion of the vasoconstrictor centre was present, fall of arterial pressure occurred. Nor was the fall necessarily due to relaxation of the arteries, because the blood was not at rest. Relaxation would give a fall only in the large arteries, not in the smaller such as the radial. He(29, 39, 57, 58) suggested that contraction of the small arteries might produce the fall of blood pressure. He believed that as the vessels contracted the B.P. in them decreased. As the small arteries had a regulating or "stop-cock" action on the blood-flow, contraction of the arteries proximal to the regulating point gave an increased B.P., but of those distal a

lowered blood pressure.

Besides the nervous regulation of the blood-supply, it is probable, as suggested by Bayliss, that chemical regulation exists in the smallest arterioles (see Dilatation of the Capillaries). On the one hand, acids in slight concentration, as shown by Gaskell(1), e.g. lactic acid in muscle,  $\text{CO}_2$  as shown by Bayliss(19), and Hooker (122), give vascular dilatation and may thus supply more blood where it is needed. Similarly, nitrites therapeutically. On the other hand, adrenin and pituitrin cause vasoconstriction, and thus tend to maintain normal vascular tone. It is probable, indeed, that adrenin is increased in Traumatic Shock as a protection against lowering of blood pressure (see CHANGES IN THE ADRENAL GLANDS).

Is this dilatation of the small arteries actually present in Traumatic Shock?

#### Facts of Clinical and Experimental Observation.

The simplest and most direct method to prove this is obtained by mere INSPECTION. When observations were made to see whether arterial dilatation was present, it was found absent. Clinical observations in Operative Shock by Malcolm(4, 29, 33, 39, 40, 57, 58, 582) in 1893 indicated that the arteries were contracted, and that, after operations, though the pulse and blood pressure were good, nevertheless, shock might develop. Indeed, the clinical picture of shock, viz. pallor of the skin and abdominal viscera, lowered surface temperature, small

pulse, and lowered B.P., scanty bleeding, anuria, suggested to Malcolm that the vasomotor system might be intensely active.

Sweating and dilatation of the pupils indicated, as Cannon(260) suggested, that the sympathetic system was active.

In abdominal operations in Wound Shock, no dilatation of the splanchnic vessels was observed by surgeons(240, 474). Absence of radial pulsation, and of bleeding from the cut vessels, might be associated, with pulsation in the larger arteries. The veins also appeared to Rendle Short(424) to be contracted, and he found that it might be difficult to insert the transfusion needle.

Nor did facts from Experimental Shock tally with the supposition. The arteries were found empty in Crile's experiments(16, 560). The retinal blood vessels were observed by Seelig and Lyon(98) to be markedly contracted.

These facts, then, demonstrate that dilatation of the small arteries is absent in shock, at least in the stages of shock in which the observations were made, and, accordingly, the tonic activity of the vasoconstrictor fibres is not lost altogether. Complete exhaustion of the vasoconstrictor centre, therefore, is not present and cannot be the cause of shock. The above method, however, does not give quantitative data. Some exhaustion of the centre may still be present. The arteries may still be relaxed somewhat, but empty, the blood having flowed on into the veins, according to Crile(655) in 1923.



Crile(14,15,560)had found that,if stimulation of sensory nerves were often repeated,the pressor reflex effect got less and less,until none was obtained,or even a depressor effect.Similarly,with the injection of strychnin in often-repeated doses.

Porter(22,44,45,46,47)was the first to test the validity of the above hypothesis by experiments. The method he used was indirect,and consisted in testing qualitatively and quantitatively the pressor and depressor reflexes in shocked animals. The fall of arterial pressure from stimulation of the depressor nerve,and the rise of pressure from stimulation of other afferent nerves were proportionately as great in shocked as in normal animals.E.g.,stimulation of the central end of the depressor nerve in a shocked animal gave a 40 % fall of B.P.,which was as great as in the normal animal. Stimulation of the central ends of the brachial or sciatic,even for many hours,still gave a pressor effect. Practically no diminution in the response took place until the B.P. had fallen to a  $\frac{1}{3}$  of the original height, and the reflex only failed when the B.P.had fallen so low that anaemia of the centre was certain.In fact, proportionately,the percentile rise of B.P. increased as the B.P. fell.In gross mechanical injuries of the brain,Porter(44)found,the vasoconstrictor reflexes were increased,probably from concurrent impulses from the injured tissues.

Seelig and Lyon(64,98)confirmed these results by

testing the pressor action of the vagus in dogs, after removal of the stellate and coeliac ganglia so as to cut off the accelerator nerves. On stimulation of the central end of the cut vagus with the other vagus divided, they found that the rise of B.P. was proportionately greater than in the normal animal. These results were also confirmed by Mann(142), and by Janeway and Ewing(148).

Sollman and Pilcher(94), however, obtained the same results as Porter, but interpreted them differently. For blood pressures between 70 and 160 mms. of Hg., the absolute rise was the same. The percentile rise, therefore, varied inversely to the level of B.P., and the response of the vasoconstrictor centre did not bear any simple relation to the B.P.. They considered that the absolute rise was a more correct index of the degree of vasomotor response than the percentile change. The vasoconstrictor centre did not, then, react more powerfully to sciatic stimulation at low pressures.

Guthrie(255, 349, 366) also found that, on strong repeated stimulation of the brachial, the pressor effect diminished after a time, and in profound shock both the vasomotor and respiratory reflexes were profoundly decreased. The decrease in the pressor effect was both actual and percentile. But interpretation of these reflexes he thought was difficult.

Wiggers also obtained similar results(372) to those of Porter. At the onset both pressor and depressor reflexes took place. After each crushing of the testes

depressor effects were obtained, along with acceleration of the heart, and acceleration and augmentation of the respiration, and consequent increase in effective venous pressure, and on cessation of the stimulation, the B.P. returned to the normal level. But after repeated crushing, the recovery was less and less.

Again, Seelig and Joseph (146) experimented on rabbits in which the superior cervical ganglion had been removed and the Great Auricular Nerve cut 24 hours previously. In abdominal shock, the normal ear remained blanched, the denervated ear slightly flushed. If the aorta were clamped to get a sudden rise of arterial pressure, the arteries of the intact ear still remained constricted, those of the denervated ear became distended, but the distension was less than in the normal animal. Similar results were obtained by Mann (142) for the arteries of the dog's tongue, the rabbit's ear, the kitten's or puppy's paw, and the renal arteries.

Direct chemical excitation by increased Hydrogen-ions, Mann (142) found, had a marked effect on the vasoconstrictor centre in shock. He stimulated the centre by asphyxia, caused by an artificial pneumothorax, inhalation of a high percentage of Carbon Dioxide, or increased intracranial pressure, and found as great a rise of B.P. after shock was produced as before.

These experiments, then, show that the vasoconstrictor centre is not completely paralysed, and that it still has some degree of activity. A percentile rise of B.P., however, may still denote some loss of activity in the

centre, for an intact centre should be capable of giving an unimpaired absolute rise. The centre may be overactive and unable to keep up the B.P.. It may effect only a small additional, but still percentile rise.

These experiments have limitations. They only prove for this one variety of shock due to stimulation of afferent nerves, not for all kinds of shock. They are, moreover, indirect methods.

#### VARIATIONS IN THE ARTERIAL AND VENOUS PRESSURES.

Seelig and Lyon (98) found that, in Experimental Shock, along with increase in venous out-flow from the femoral vein the venous pressure was increased.

Wiggers (365, 372) concluded from his study of the dynamics of the circulation, that, in the initial stage, there was a diminished peripheral resistance from the fall of arterial pressure and the gradual rise of venous pressure. But, in the progressive stage (or in severe shock from the first) the venous pressure fell very rapidly and at the end became very low.

In man the venous pressure may be estimated most simply, according to Howell (625), by the method of Gaertner. The extended arm is raised slowly until the veins of the hand just disappear. The height above the costal angle gives the venous pressure in the right auricle.

#### PLETHYSMOGRAPHY.

By observations on the volume of the dog's leg, Muns (190) studied vasoconstrictor tone. In Experimental Abdominal Shock under ether, the leg-volume showed an im-

immediate fall with the fall of blood pressure, sometimes returning to normal, then undergoing a gradual fall, which continued as long as the stimulation lasted, and amounted to 2-10 ccs.. When manipulation ceased, the volume rose; when manipulation was resumed, it fell. The arterial pressure was maintained throughout, or even rose above normal. When vasoconstriction was absent, the B.P. tended to fall; when vasoconstriction was present but slightly, the B.P. was better maintained; when vasoconstriction was marked, the B.P. was better maintained, or even raised. Therefore, increased vasoconstrictor tone helped to maintain the B.P., and was probably raised in the early stage. These results were probably explained by the variations in normal degree of vasoconstriction, as the vasoconstrictor centre was probably not a variable factor. If the normal vasoconstriction was good, the B.P. was maintained or even raised, but if weak or absent, the B.P. tended to fall.

the case of

In Mechanical Shock, produced by a 2-hour partial occlusion of the Inferior Vena Cava, Janeway and Jackson (191) studied the volume of intestinal loops. At first during the occlusion, vasoconstriction took place along with a fall of arterial pressure, then the vasoconstrictor tone was decreased, but not lost. The tone varied directly with the arterial pressure. In a 2-hour partial occlusion of the aorta, the vasoconstrictor tone was decreased during occlusion, but increased even beyond normal during deocclusion, though the arterial pressure was low, and then later it was decreased. The tone was



generally only normal, when the B.P. was low, instead of being above normal. These results were confirmed by Erlanger(256,257,456,458,460), and by Cattell(614).

BY MEASURING THE OUT-FLOW OF BLOOD FROM THE VEINS, vasomotor effects may be determined. Decrease in flow of blood from the veins implies vasoconstriction. Seelig and Lyon(64,98) observed that, in Experimental Shock, increase in blood-flow from the femoral vein, after section of the sciatic nerve, was greater than in the normal animal, i.e. vasoconstriction was increased. This result was confirmed by Mann(142), and by Guthrie(255), who found 22 % increase before, and 76 % after shock.

#### ARTIFICIAL PERFUSION.

This method was used by Sollman and Pilcher(94) to eliminate the simultaneous cardiac effect, the passive effect, and the action of drugs such as adrenin. They used the spleen of dogs, sometimes the kidney. The arterial connections were severed, and the nerves left intact. The vagi were divided. Slowing of the out-flow corresponded to vasoconstriction. Maximal stimulation of the central end of the sciatic gave a decrease of 20 %. Direct stimulation of the centre by asphyxia continued to give a marked vasoconstriction, as the B.P. fell, even for a few minutes after death(102). Similar results were obtained in the case of haemorrhage(see CAUSAL FACTORS—Haemorrhage). Bayliss(241), using a similar method of artificial perfusion of the limb of a cat, also found that a fall of arterial pressure produced

peripheral vasoconstriction through the nerves.

Morrison and Hooker(188)also found that,in the perfusion of the blood vessels of organs,the out-flow from the veins was decreased,after shock was produced. If the nerves were severed,the out-flow was increased. The stage of shock was not mentioned,and in these experiments great disturbance of the vascular area was inevitable,and probably the tissue cells were injured or destroyed by contact with the perfusate.Hence,as Belt,Smith,and Whipple(489)pointed out,deductions must allow for this.

INFLOW INTO THE ARTERIES was measured by Bartlett(123).

The average rate of intermittent inflow of salt solution under constant pressure into the femoral artery of a dog was measured.Decrease in rate implied vasoconstriction.The rate was 36 % faster in shock than in the normal dog,i.e.the vasomotor tone was decreased. The increased rate didn't begin till after the fall in blood pressure had started.The increased rate was not due to the venous or collateral arterial circulation, because the pressure was high enough to nullify such effects; and the amount of saline used ( e.g.100 ccs. in 3 hours ) was too small to affect the B.P..

Erlanger and his coworkers(257,454)confirmed these results in the case of Experimental Abdominal Shock. The inflow rate at first was normally reduced,then gradually increased,i.e.the vasoconstrictor tone was at first increased,but,after the arterial pressure had fallen to 50 millimetres of mercury or so,the tone

had become subnormal, though it was never entirely lost.

In experimental shock, induced by temporary partial occlusion of the Inferior Vena Cava, similar results were obtained by Erlanger and his coworkers (257, 456). During occlusion, vasoconstriction was associated with rise of venous pressure and fall of arterial, and was probably caused by the anaemia thus produced. Later, the tone gave way, probably from depression of the centre by the anaemia. During deocclusion, the vasoconstrictor tone increased, along with the rise of arterial pressure, and often continued to increase after the arterial pressure had begun to fall, but eventually it underwent a slow decrease, probably from the exposure of the animal and diminished blood supply. After the B.P. fell to 50 mms. of Hg., both rapidly declined, but some residual tone remained. The constriction was less than it should be in the normal animal. With low arterial pressure, the constriction was only at the normal level instead of higher, because the vasoconstrictor centre was somewhat depressed. In temporary partial occlusion of the Thoracic Aorta, the vasoconstrictor mechanism was efficient.

Cannon (438, 614, 616) obtained results confirming those of Bartlett and Erlanger. He used a method of controlling the arterial pressure by varying the pericardial pressure. By means of a funnel and cannula, filled with saline and connected to the pericardial sac, he could artificially compress or release the heart, and so decrease or increase the arterial pressure. If the B.P. were held

at 60 mms.Hg. for 1 hour, and then the compression released, complete restoration of B.P. at first took place, but became less and less with each succeeding test. Vasodilatation did not occur until the average B.P. had been reduced to 65 mmsHg.. This downward tendency was not due to loss of blood volume, as shown by the haematocrit readings. Therefore, probably the nerve centres were damaged by inadequate circulation.

Summary. In the initial stage of Delayed Shock, the tonus of the vasoconstrictor centre is increased and the small arteries are dilated. As shock progresses, the tonus drops back to the normal level, and then gradually declines. Even in the advanced stage, the tonus still exists.

Conclusion. Exhaustion of the vasomotor mechanism is not the cause of Traumatic Shock. The tonic activity of the vasoconstrictor fibres, as determined by the condition of the small arteries, etc. is apparently not decreased in the early stages, and accordingly complete paralysis of the vasoconstrictor centre is not always present in shock, and therefore cannot be the cause.

The tonic activity of the centre appears to vary in the different stages of shock. At the time of injury, it may show a temporary inhibition, i.e. in Immediate Shock. In the initial stage of Delayed Shock, it may be more active. This hyperactivity continues as long as the B.P. remains up, but later after the B.P. begins to fall, the vasomotor tone is decreased, and when the B.P. has fallen to about 50 mms. Hg., the tone is definitely subnormal.

Even at the end, some slight residual tone remains. The tone, then, does not vary directly with the arterial pressure. It may be increasing when the pressure is falling, and may be above normal when the pressure is below normal. The failure of vasoconstrictor tone is not, then, the cause of the low B.P..

In the case of Traumatic Shock, due to exposure and manipulation of the abdominal viscera, however, dilatation of the small arteries (veins and capillaries) probably occurs and in part causes the fall of B.P. (see SUPPOSED DILATATION OF VEINS).

#### WHAT IS THE CAUSE OF THIS VASOCONSTRICTION?

The activity of the vasoconstrictor centre in the medulla is generally supposed to be the cause, both by reflex stimulation and by its tonic activity.

Other factors are the spinal vasomotor centres, the tonicity of the skeletal muscles, the heart beat, and the tonicity of the blood vessel walls themselves.

Pike and his coworkers (121, 138, 669) found that with the spinal cord removed there was a residual blood pressure, equal to 33 mm of Hg.. This residual B.P., with the spinal cord transected, or after elimination of the bulbar mechanism by anaemia, transection of the lower cervical spinal cord, or by decerebration and later transection, was greater than that after complete removal of the spinal cord. This residual B.P. was due mainly to tonic contraction of the skeletal muscles, for under curare it was slight. The spinal vasomotor centres played some part also, as well as the autonomic



nervous system. Probably, then, the vasomotor centre controlled the B.P. normally, but, when it was in abeyance, the shorter connections might be established through segments of the spinal cord.

Chemical agencies may be operative also to some extent. The increased secretion of adrenin, e.g., which probably occurs in the initial stage, may help to produce vasoconstriction and thus maintain the normal vascular tone.

#### WHAT IS THE SIGNIFICANCE OF THIS VASOCONSTRICTION?

It would seem, therefore, that the vasoconstrictor centre counteracts the fall of B.P. by increased action, and so is another instance of a protective mechanism. The vasoconstriction of the small arteries tends to diminish the capacity of the vascular system, and so maintain the progressively falling B.P.

The converse is seen in the pharmacological action of digitalis on the B.P.. An increased efficiency of the heart is compensated by a slight diminution in the tone of the vasoconstrictor centre, which reduces the peripheral resistance and gives a greater flow of blood. The increased volume flow of blood to the brain causes this reduction in tone, according to Cushny(177).

As the blood pressure falls and the blood supply of the centre fails, the action lessens, and at last it may be unable to respond. Pike, Guthrie, and Stewart(54), however, concluded from a study of experimental cerebral anaemia, that the vasoconstrictor centre was probably more resistant than the respiratory centre, as it failed

gradually and began to function sooner on restoration. The loss of tone, then, is the result, and not the cause, of the low B.P..

In Experimental Shock, when stimulation of a sensory nerve fails to give the usual pressor effect, the tonic activity of the centre may be maximal. It is already constricting the small arteries as much as possible in the effort to compensate for the fall of arterial pressure. No increase occurs because the small arteries are already constricted to the utmost.

#### (b). SUPPOSED DILATATION OF THE VEINS.

It is known that the veins also are capable of dilatation or contraction through the vasomotor fibres or local chemical stimuli.

Formerly it was generally supposed that fatigue of the vasoconstrictor centre was the cause of shock, and that consequently dilatation of the splanchnic blood vessels resulted. Decrease of venous tone due to ascapnia was suggested by Henderson(96) in 1910. When, however, the facts as to the condition of these vessels were ascertained by direct inspection of the abdominal cavity in Delayed Shock, it was found that the vessels of the peritoneum were not dilated, unless manipulation of the viscera had been done. It seems still possible, however, that Immediate Shock may be caused in this way. The nature of this condition probably closely resembles syncope, in which a reflex nervous inhibition of the medullary nerve centres is supposed to take place, and

result in cardiac inhibition,vascular dilatation of the somatic and splanchnic areas,relaxation of muscle tone, etc..Goltz found in 1863 that rapid light taps on the abdomen of the frog caused standstill of the heart and dilatation of the splanchnic blood vessels,and there is much evidence,both clinical and experimental,to show that stimulation of sensory nerves causes these <sup>reflex</sup> changes. By analogy it was inferred that Immediate Shock resulted in the same way.

#### FACTS OF OBSERVATION.

##### (1).INSPECTION.

Direct inspection of the abdominal veins during Traumatic Shock usually revealed no dilatation. During abdominal operations in Wound Shock cases,Wallace,Fraser, and Drummond(240,474)found no dilatation of vessels. In the case of Experimental Shock in animals,observers, including Gasser and Erlanger(454,458)found no dilatation, unless handling of the abdominal viscera had been done.

R.Short(424)described contraction of the superficial veins as seen when doing transfusion in cases of Wound Shock.

In the older experiments,however,in which Experimental Traumatic Shock had been produced by manipulation of the intestines,the abdominal or splanchnic veins were observed to be distended.In Crile's experiments(16,563), the veins were full and distended,in contrast to the empty arteries and heart. Dissection and autopsies both showed a general venous engorgement as in death from other causes.These changes,Malcolm(4) pointed out,

resembled inflammation. Mann(195) had found, too, that the specific gravity of the blood in the portal vein was increased.

## (2). ESTIMATIONS OF THE AMOUNT OF BLOOD IN THE SPLANCHNIC CIRCULATION.

Morrison and Hooker(188) also found that, in Experimental Shock, due again to exposure of the abdominal viscera, the weight of an isolated loop of gut was increased, and the portal pressure decreased. They, therefore, supposed that the splanchnic veins were dilated in shock and contained the lost volume of blood.

On the other hand, Guthrie(255) estimated the proportion of blood in the abdominal viscera after death from Experimental Shock, produced by brachial nerve stimulation, followed by amputation of a fore limb or exposure and manipulation of the intestines, and found it only a seventh of the whole.

In all these experiments, however, a fallacy had existed. The mechanical irritation itself from the manipulation of the intestines would cause this congestion of the arteries, veins, and capillaries, or possibly, as Mann(502) suggested, the changes in abdominal pressure or venous obstruction might be partly responsible.

## (3). VENOUS BLOOD PRESSURE.

In the initial stage of Traumatic Shock, according to Wiggers(365, 372), the venous pressure was gradually increased, but in the progressive stage (or in severe shock from the first) it fell rapidly, and at the end became very low.

The portal, as well as the systemic, venous pressure, Morrison and Hooker(138) found, also fell, but the jugular venous pressure remained practically unchanged. These changes indicated that the heart was able to pump on all the blood that came to it. The slight difference in pressure between the blood in the peripheral veins and in the Superior Vena Cava, estimated by Henderson and Barringer(134) at 5 mms. of mercury, was sufficient to drive the blood into the heart and fill it during diastole. The portal venous pressure, however, Gasser and Erlanger(454, 466) observed, might sometimes be elevated (as in adrenin and caval shock), sometimes lowered (as in intestinal exposure and aortic occlusion).

Summary. Apparently, then, both dilatation and contraction may be present in Traumatic Shock. (1). Dilatation of the splanchnic veins is apparently present in the case of Traumatic Shock due to intestinal manipulation. (2). Contraction of these vessels appears to be the usual condition in other kinds of Traumatic Shock.

In addition to abdominal shock, however, splanchnic dilatation may be present in Immediate Traumatic Shock. Bayliss(308) suggested that it might be present even in the initial stage of Delayed Shock, being a peripheral reflex, and starting the consecutive processes. Fraser(474), moreover, suggested that the veins behind the contracted vessels of the peritoneum might be dilated and yet invisible to inspection. The obstruction offered by the double system of capillaries, and the low B.P. in the portal circulation would favour it mechanically.



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In addition, the hepatic vessels might contract early in shock from their vasomotor control.

If splanchnic dilatation be present, fall of blood pressure is present, other factors being equal. Produced by section of the spinal cord or splanchnic nerves, it tends to lower the B.P.. Janeway and Ewing (148) found that, combined with prolonged stimulation of the afferent nerves, it produced Traumatic Shock. Stimulation of the brachial or sciatic alone for 2 hours failed to give a significant fall of B.P.. But if the great splanchnic nerves were first cut, (or if severe bleeding were done, or if the ether anaesthesia were prolonged), then a significant fall of B.P. and other signs of shock appeared. If the splanchnics were then stimulated, no rise of B.P. and no change in the plethysmograph took place. Produced by clamping the portal vein, splanchnic dilatation, Cannon (260) found, gave a fall of B.P., just as in haemorrhage. Erlanger and his coworkers (257), however, found that clamping the Inferior Vena Cava was more effective.

On the other hand, if splanchnic dilatation be present, the dilatation may be compensated, and no fall of B.P. may be produced. Gasser and Erlanger (257) found that with a high portal pressure shock might not be produced.

If splanchnic dilatation be absent, fall of B.P. may still develop. Gasser and Erlanger (454, 466) pointed out that, though in "adrenin" and "caval" shock the portal pressure was elevated, yet in shock from intestinal exposure and "aortic shock", it was lowered. If splanchnic dilatation

were prevented by ligation of the Thoracic Aorta or of the abdominal vessels, or by distending the intestines with air so as to drive out the blood, then trauma could still produce shock according to Crile(563). Moreover, Cannon(260) pointed out, attempted elimination of this factor by treatment, such as lowering the head, bandaging the abdomen, intraperitoneal injection of pituitrin, had less effect on shock than it would be expected to have. Similarly, in eviscerated animals or after excision of the abdominal sympathetic and section of the splanchnic nerves to cut off vasoconstrictor stimulation, shock developed in the same way or even faster, according to Gasser and Erlanger(257,454). Vasoconstriction, as determined by the in-flow rate into the arteries, was even more marked than without such procedures.

Conclusion. From these facts it appears that splanchnic dilatation <sup>when present</sup> is not an essential causal factor, and that the splanchnic area is not more important than any other area of the same size.

#### WHAT IS THE CAUSE OF THESE CHANGES OF CALIBRE IN THE VEINS?

In the case of the more usual constriction, two main agencies may be concerned, viz. (1) venomotor fibres, (2) local chemical stimuli.

In the case of the splanchnic dilatation in "abdominal shock", presumably the local mechanical irritation, due to either the exposure or the manipulation or both, produces the change. This physical stimulation may produce effects through the above agencies, and in addition

(3) passive changes may be responsible.

(1) VENOMOTOR NERVES.

Mall(7) showed in 1896 that the portal vein was supplied with vasoconstrictor fibres from the splanchnic nerves, and similarly other veins are probably controlled in the same way. E.g. Hooker(374) demonstrated that in the veins of the large intestine rise of blood pressure might be obtained by direct or reflex nerve stimulation.

(a). The venoconstriction probably results mainly from excitation of the constrictor fibres, as in the case of the arteries.

(b). The venodilatation, on the other hand, may result either from stimulation of the venodilator fibres, or from inhibition of the constrictor fibres, due in either case either to a central reflex through the splanchnics or a peripheral axon reflex. Webster(129) concluded it arose from a central reflex, because it still occurred after section of both vagi, and it was moreover a transient effect and not clearly connected with shock. Hooker(374) showed experimentally that contraction of intestinal muscle might probably produce changes in the venous pressure.

Mann(502) suggested local inhibition of vascular tone or local active vasodilatation.

Y. Henderson(96, 373), on the other hand, pointed out that the veins were not nearly so readily influenced as the arteries by nerve stimulation. E.g., after the vagi were cut, stimulation of the splanchnics (or injection of